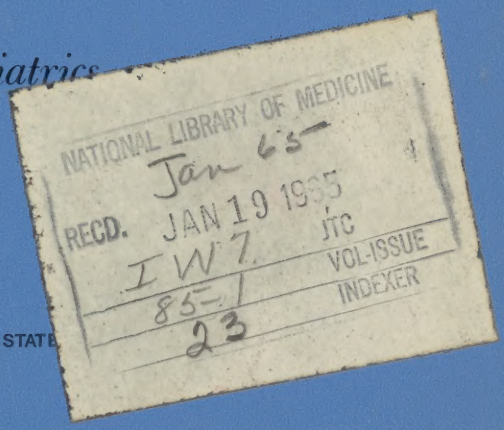
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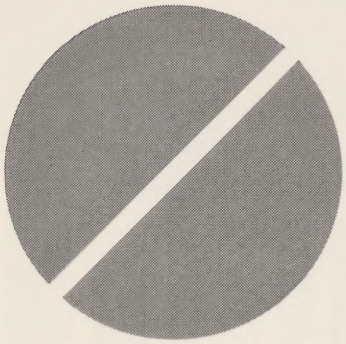
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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, *22*:527, 1964.

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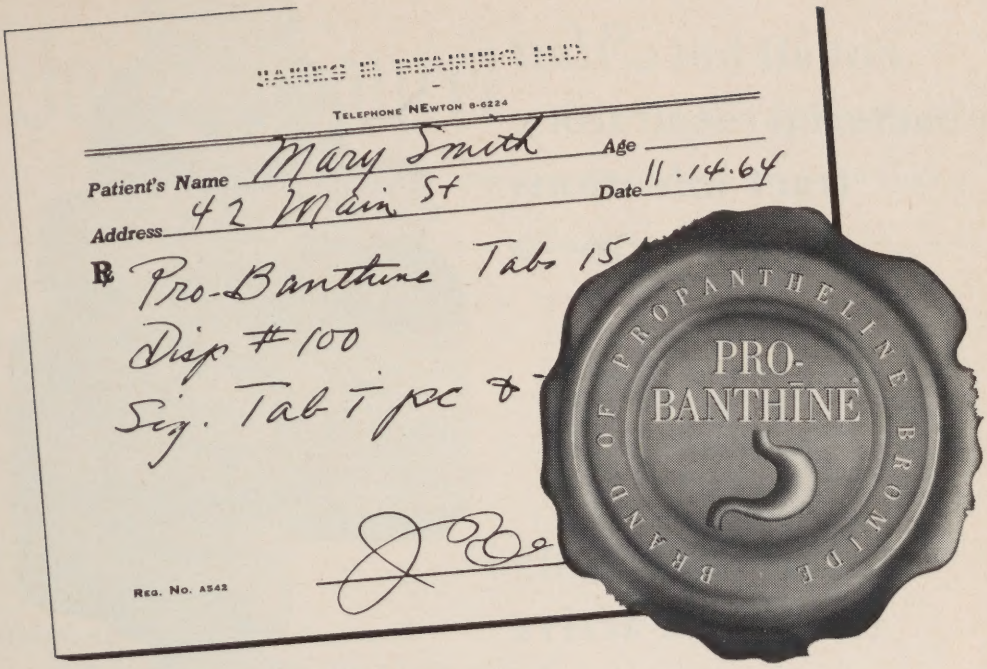
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Second class postage paid at Minneapolis, Minn. Publication office: 65th at Valley View Road, Southdale Park, Minneapolis, Minn. 55424. Printed in U.S.A. Published monthly. Subscriptions: $5 a year, 50 cents a copy (special issues $1 a copy). Louis M. Cohen, Publisher; Allan Stone, Assistant to the Publisher.

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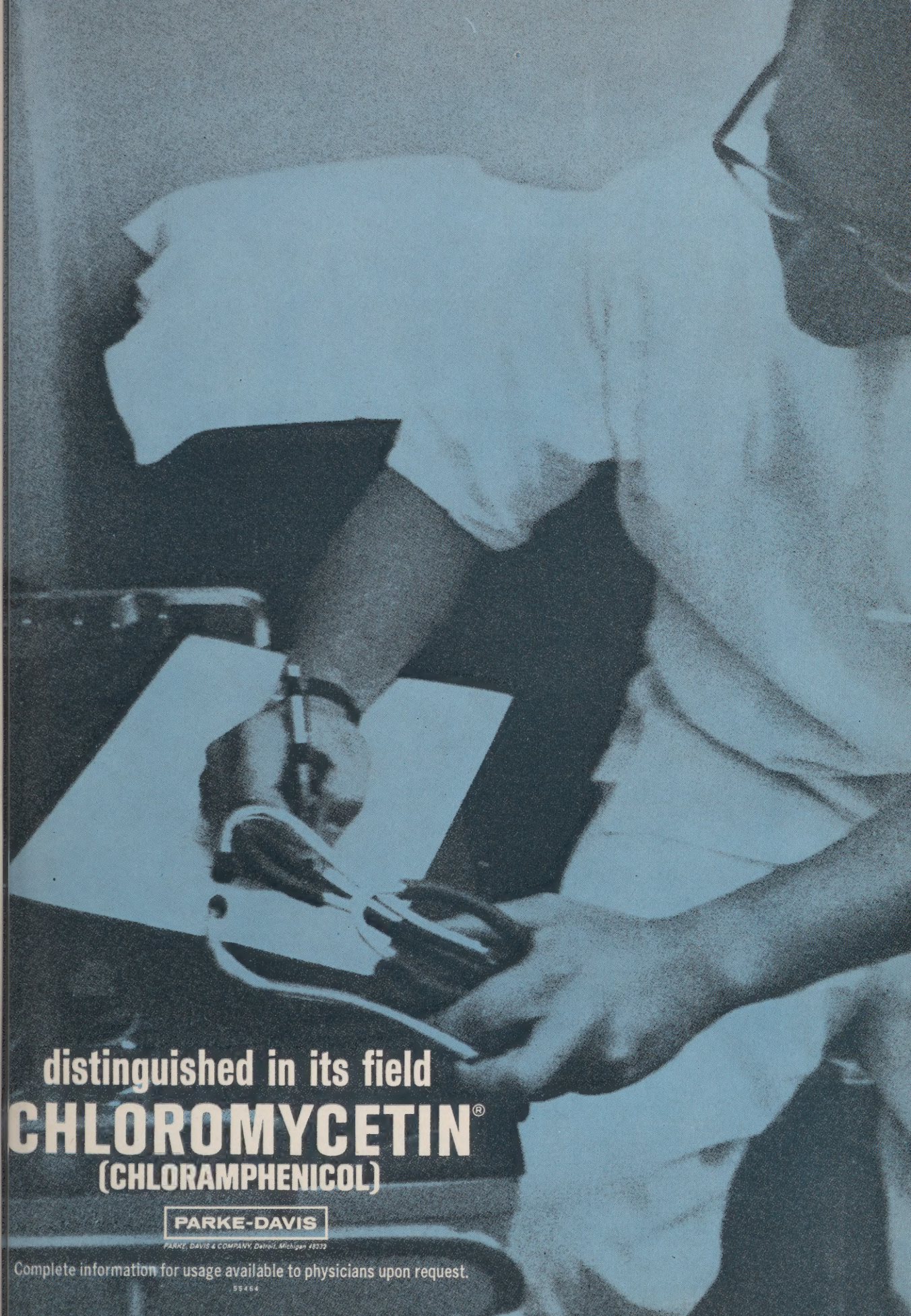
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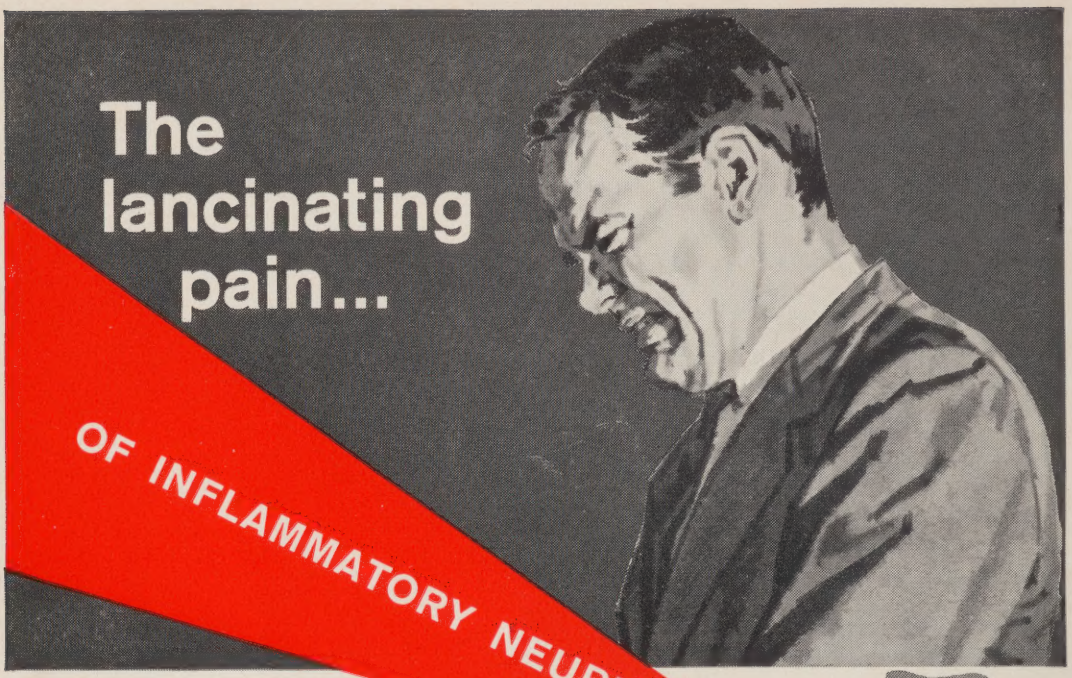
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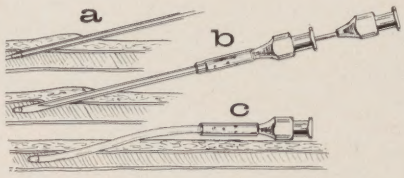
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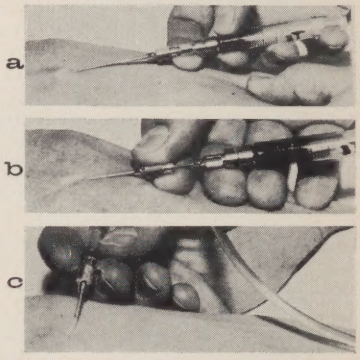
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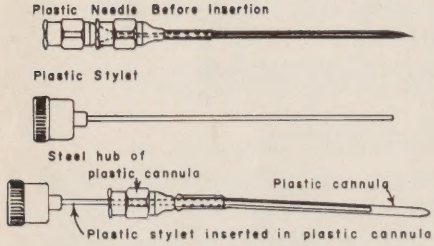




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The first unauthenticated accounts of free skin grafts were used by the Hindus in 1800 B.C., according to Donald L. Lamb, M.D., Fargo, North Dakota. Writing on "Indications for the Use of Split- and Full-Thickness Skin Grafts," the lead article to appear in the February issue of THE JOURNAL-LANCET, Dr. Lamb states that the first free graft was reported in this country in 1840 and was performed by Jonathan Mason Warren in Boston. By 1886, Thiersch had had successful grafts with large split-thickness grafts, and by 1875 Wolfe reported success with full-thickness grafts.

Since these pioneer developments, there have been many advances in this field. Dr. Lamb defines the types of free grafts now available, explains the indications for the use of the various types of grafts, and discusses some of the important technical features in the successful application of these grafts.

The seven basic types of skin grafts are carefully considered: thin split-thickness, thick split-thickness, full-thickness, composite, flap, neurovascular or vascular island pedicle flap, and the still experimental, free island flap grafts.

Among other papers to appear in February are:

- **The Natural History of Tuberculosis in the Human Body,** by J. Arthur Myers, M.D., Minneapolis.
- **Tracheostomy,** by Theodore J. Scharf, M.D., and Daniel E. Smith, M.D., Albuquerque.
- **Ethchlorvynol Intoxication and Severe Abstinence Reaction,** by John L. Magness, M.D., Fargo.
- **Winter Sports Injuries,** by Mark B. Coventry, M.D., Rochester, Minnesota.

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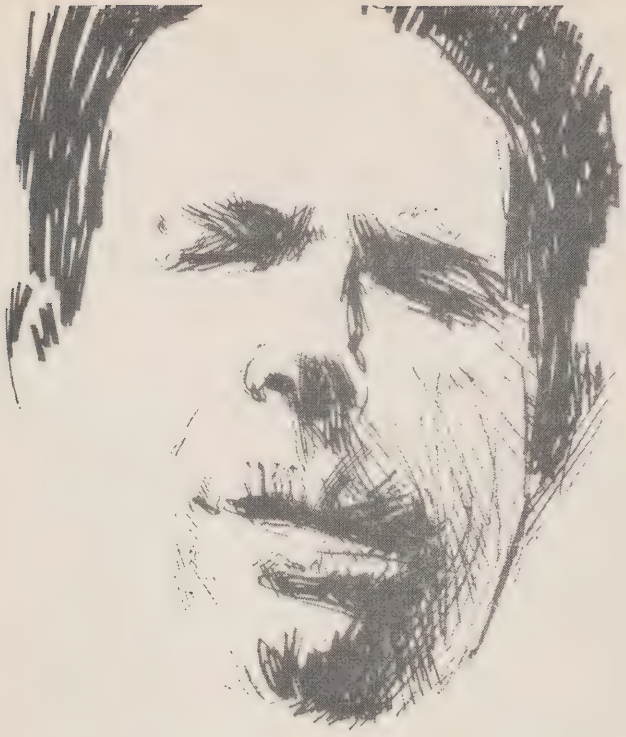
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Editorial

THIS special issue of THE JOURNAL-LANCET introduces the first of a series devoted to the field of pediatrics. THE JOURNAL-LANCET for ninety-six years has been an effective instrument for the communication of the broad aspects of medical knowledge directed primarily to the practicing physician and specialists in the central part of the United States and Canada. From time to time special issues devoted to selected medical, pediatric, obstetric, or surgical subjects have appeared. These have been well received not only by physicians in the central part of the United States but by physicians and medical educators throughout the United States as well as in many foreign medical centers.

This splendid series of papers from the Department of Pediatrics at the State University of Iowa, prepared under the direction of Dr. Donal Dunphy, professor and chairman of that department, represents the first of these special issues which will be forthcoming from pediatric, clinical, and research centers in the midcentral United States and Canada. These issues will appear at intervals of three or four months throughout the years 1965 and 1966. Forthcoming special issues are being prepared by Dr. Cyrus Peterson, professor and head of the Department of Pediatrics of Marquette University at Milwaukee, Wisconsin; Dr. Harris D. Riley, professor and head of the Department of Pediatrics at the University of Oklahoma; Dr. Theodore Panos, professor and head of the Department of Pediatrics at the University of Arkansas; Dr. Gordon E. Gibbs, professor and head of the Department of Pediatrics at the University of Nebraska, Omaha; Dr. Harry Medovy, professor and head of the Department of Pediatrics at the University of Manitoba, Winnipeg.

This issue from the State University of Iowa is representative of those to follow in that an appropriate balance of clinical research and basic research subjects has been presented. It is hoped that these issues will effectively identify the breadth and the depth of medical problems of importance to the welfare of infants and children as well as to portray the high standards of clinical and research activity taking place in the medical school centers in central portions of the United States and Canada.

JOHN A. ANDERSON, M.D.

JOHN A. ANDERSON *is professor and head of the Department of Pediatrics, University of Minnesota Medical School, Minneapolis.*

Ataxia in Childhood.

Clinical Approach and Differential Diagnosis

WILLIAM E. BELL, M.D.
Iowa City

Ataxia when viewed broadly refers to incoordination of movement or a disturbance of balance. The physician confronted by a child with ataxia is faced with a long list of possible explanations as this represents a physical sign that may result from dysfunction of a variety of anatomical structures. To complicate even more the diagnostic difficulties is the fact that incoordination of gait, for example, can be a manifestation of structural pathology, a pharmacologic process, or even a psychiatric disorder. This discussion deals primarily with neurological diseases of childhood producing ataxia. However, before one initiates an extensive diagnostic survey in this area it is wise to consider and exclude other possible factors, especially if the disturbance mainly involves the patient's gait. Hip joint disease may cause a marked alteration in the child's ability to ambulate and is at times confused with neurologic disease. Very young children who are not yet able to relate symptoms verbally may show an alteration in gait because of a painful disorder, such as foreign body of one foot, identified only by careful examination.

Certain neurologic disorders although not classified generally among the ataxic group may be presented to the physician with the complaint of clumsiness, frequent falling, or stumbling. Not infrequently youngsters with progressive muscular dystrophy are referred with the parent's description of incoordination and falling, with no awareness of weakness. The clumsiness in such a child is the result of weakness of the lower extremities and pelvic girdle, and not due to any of the central neural mechanisms related to coordination or synergy. Identification of muscle weakness, along with diminution of deep tendon reflexes and frequently calf pseudohypertrophy, helps orient the examiner, leading to correct diagnosis. Observation of the child with muscular dystrophy as he rises from the sitting to the standing position is of considerable value as the muscle weakness is reflected by his need to assist himself in rising with the use of his upper extremities. The child with spastic lower extremities may also appear to have gait incoordination; however, the physical findings of spasticity including increased tone to passive movement, hyperreflexia, clonus, and pathologic toe signs quickly permit differentiation here. Difficulty may be encountered diagnostically, however, in those disorders where spasticity is associated with cerebellar disease, as occurs in rarer forms of hereditary degenerative disease.

Although not totally true, we conventionally relate ataxia of central nervous system origin to a disturbance of structure or function of the posterior columns of the spinal cord or of cerebellum and its efferent and afferent pathways. Cerebellar ataxia may be classified in a general fashion as to the major site of involvement. The midline or cerebellar vermis syndrome is reflected by the resulting dysfunction of the flocculonodular lobe of the posterior vermis. This portion of the vermis is functionally related to the vestibular system and thus with trunkal equilibrium. The cerebellar vermis syndrome is clinically manifested by swaying of the body or staggering with little involvement of limb function if the trunk is fixed. Axial or trunkal ataxia is often noted by swaying or gradual tilting of the trunk while the child is sitting. When minimally present, one may observe little in this regard until funduscopic examination is attempted, and then with increased concentration by the patient there occurs a drift of his body away from the initial position. If symmetrical involvement of the vermis exists, nystagmus may not be present and

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muscle tone and reflexes may not be altered. The medulloblastoma is the classic example of the vermis syndrome in childhood. However, it should be stressed that this tumor need not, and often is not, confined to just the vermis structures. Opposed to the vermis syndrome is the cerebellar hemisphere syndrome characterized by its lateralizing features. Here the clinical findings are more appendicular than trunkal and the abnormalities occur on the same side as the diseased cerebellar hemisphere. Dysmetria, dyssynergia, hypotonia, and hyporeflexia are found in the involved extremities. A gross disturbance in discreet and skilled movements of the hand may be seen without appreciable loss of strength. Nystagmus is usually present. The cystic cerebellar astrocytoma is the example usually cited of the hemisphere syndrome in childhood. While this dichotomy of cerebellar syndromes is made, it is important to emphasize that in practice most diseases affecting the cerebellum involve in varying extent different portions of its structure and do not necessarily confine themselves to either vermis or hemisphere. Thus, mixtures of these two patterns are more often encountered. If due to neoplastic disease, the ataxia is usually associated with other findings such as those of increased intracranial pressure. Sensory ataxia due to spinal cord disease is a less commonly encountered problem in pediatric neurology than in adults. The disturbance in coordination in states associated with posterior column involvement results from loss of the proprioceptive clues from the lower extremities which provide information to higher centers about the position of the body relative to space and environment. This type of ataxia is aggravated when visual clues are also removed as manifested by the increased disturbance such patients have in a dark room or with their eyes closed. The ataxia occurring in the familial disorder, Friedreich's ataxia, is in part due to posterior column involvement but is compounded by a cerebellar component as well. Spinal sensory ataxia is identified by the finding of proprioceptive abnormalities such as position sense and vibratory sense testing.

The comments above illustrate the necessity for a detailed neurologic examination in order to identify the type of problem and probable site of disease. Concerning tests for coordination and equilibrium the approach must be varied according to the age of the child. In older children where cooperation is present the usual procedures such as finger-to-nose, heel-to-knee, observation of gait, and Romberg testing are available. Experience has shown that even bright children may have difficulty understanding what is desired by the examiner on the finger-to-nose test. This can easily be circumvented by modifying the test slightly so that the child is instructed to move his index finger rapidly from his nose to the examiners finger, held at a distance of the child's arm-length in front of him. This demands a wide excursion of movement by the child and is nearly always done well by even young children. It is wise to test one extremity at a time in this fashion as it is simpler for the child. Concerning observation of gait, it should be recognized that mild incoordination may not be evident as the child walks but at the moment of turning he becomes slightly unsteady requiring very brief but abnormal "check movements" to prevent loss of balance. Requesting the child to turn or change directions rapidly while walking will clearly magnify this abnormality. Tandem gait testing or having him walk heel-in-front-of-toe along a line on the floor will also make minimal degrees of ataxia more evident. When the coordination disturbance is unilateral, even though little abnormality may be observed in the gait, a marked deficit is noted when the child attempts to hop on one foot. It must be kept in mind, however, that many normal children hop poorly on either foot until age 6 or 7. Testing for coordination ability is considerably more difficult to do and interpret in infants. This is partially due to the lack of cooperation naturally expected at this age plus the "physiological" clumsiness that is part of the acquisition of normal motor skills, such as occurs with learning to walk. After age 6 months, considerable information can be obtained in this regard by approaching the baby in a playful fashion and noting hand control as he reaches for objects and attempts to transfer them from one hand to the other. Tremulous movement of one hand and arm, repeated miscalculations of rate, and range of movement on one side as an infant performs may result either from paresis, ataxia, or a combination of both. Inability of the infant to stabilize his head or trunk in space while sitting or being held in the sitting position suggests trunkal ataxia. A constant titubation of the trunk or wobbling of the head is observed in such case.

Once it is established that a particular child's gait disturbance or hand control abnormality is due to ataxia, a more specific diagnosis is attempted. This may be readily apparent but ordinarily requires additional investigation including laboratory examinations, electroencephalography, a lumbar puncture, or air-contrast studies. The subsequent paragraphs outline some of the more specific disorders producing ataxia in childhood, plus the usual diagnostic approach.

TOXIC STATES

In a general pediatric or pediatric neurology practice the most commonly encountered cause of ataxia in childhood is apt to be the result of medications for convulsive disorders. Diphenylhydantoin sodium (Dilantin) is the primary offender, in part because of the magnitude of its use plus its tendency to affect the Purkinje cells[1] of the cerebellum. Ataxia may appear soon after initiation of diphenylhydantoin sodium therapy or may develop after the patient has taken the drug for many months, even without a recent change in dosage. Although intoxication may occur at almost any therapeutic dose of Dilantin, especially in sensitive individuals, quantities of 8 mg. per kg. per day may produce ataxia but does not invariably do so. The author uses diphenylhydantoin sodium in dosages of 4 to 8 mg. per kg. of body weight per day in children up to a body weight of approximately 70 pounds. Dosages less than 8 mg. per kg. per day rarely cause difficulty unless other drugs are added. Diphenylhydantoin sodium–induced ataxia is usually associated with nystagmus, either horizontal or vertical. Dysarthria is often present along with vomiting or general sedative effects. Discontinuation of the drug is followed by prompt improvement; however, caution must be taken as seizures may recur at this time. Phenobarbital, other sedatives, or tranquilizing drugs also may cause ataxia in children.

Lead encephalopathy has frequently been confused with posterior fossa tumor in childhood as both may be manifested by increased intracranial pressure and ataxia. Convulsions, however, are frequent with lead poisoning and rare with posterior fossa tumors.

Although not strictly an intoxication, the effect of heat or hyperthermia on the cerebellum might be mentioned here. Weisenburg,[2] in 1912, first described Purkinje cell damage with hyperthermia. It is now recognized that with sustained hyperthermia of 107° or over, either temporary or permanent cerebellar ataxia may result.

NEOPLASTIC DISEASE

Ataxia is a particularly prominent feature of brain tumors in childhood because of the high incidence of the subtentorial location. Any tumor located in the brainstem or cerebellum is apt to be manifested by ataxia; however, certain types of neoplasms are especially common in the pediatric years. The medulloblastoma tends to arise in the midline of the cerebellum and occurs more commonly in boys than girls. Unsteadiness of gait may be an early sign, but symptoms and signs of obstructive hydrocephalus are usually the more pronounced early features. A frequent initial symptom of this, as with other cerebellar tumors in children, is early morning vomiting. Ataxia becomes associated with nystagmus, sixth nerve palsy, eventual weight loss, or emaciation. Cystic astrocytomas of the cerebellum in childhood are more often located laterally in one cerebellar hemisphere. The ataxia is more likely to be unilateral. Because of the lateral location of the tumor, surgery is more often curative. Posterior fossa ependymomas arise and grow into the fourth ventricle. Intermittent obstruction results in episodic headaches and vomiting with ataxia occurring late, if at all. This type of cellular tumor proliferating within the fourth ventricle is apt to cause elevation of spinal fluid protein, often with a cellular response. An erroneous diagnosis of chronic encephalitis could easily be made in this instance. The pinealoma may be manifested by ataxia clinically due to its strategic location just dorsal to the midbrain. Compression on the midbrain with involvement of the efferent pathways of the cerebellum may cause incoordination. However, many other outstanding clinical features are present. The close proximity of the aqueduct of Sylvius accounts for the early appearance of obstruction with increased intracranial pressure. Involvement of the superior colliculus causes certain eye signs, including paresis of vertical conjugate gaze upward which is characteristic of this tumor. Pupils are often dilated and hearing loss may occur. The other relatively common posterior fossa tumor in children is the pontine glioma. This glial tumor occurs within the brainstem itself and is manifested by progressive involvement of cranial nerve nuclei. The fifth, sixth, and seventh cranial nerves are most commonly implicated. Long tract signs appear in the form of hypertonicity and hyperreflexia in the extremities as damage occurs to the descending corticospinal and other motor pathways. Sensory changes may be described but seem less prominent than the motor deficits. Limb ataxia develops as fiber pathways to and from the cerebellum become implicated. The brainstem glioma in childhood differs from the majority of other posterior fossa tumors in that these intrapontine lesions cause obstruction only quite late, if at all.

An additional lesion may occur in older children which closely mimics the posterior fossa tumor and may cause ataxia. Occasionally, aqueductal stenosis remains asymptomatic until the child reaches his early teens and then for reasons that are unclear, obstruction and decompensation occur. The symptoms and signs are those of increased intracranial pressure. No localizing

signs are found on neurologic examination; however, some degree of gait ataxia may be present. Ventriculography is apt to differentiate this peculiar variation of aqueductal disease from tumor; however, even posterior fossa exploration may be necessary for absolute diagnosis.

The ataxia occurring with posterior fossa tumors is one developing in a previously normal child. This variety of ataxia is progressive and is associated with other findings, usually those of increased intracranial pressure. Funduscopic examination is an extremely important aspect of the evaluation of any ataxic child. The combination of ataxia plus papilledema should preclude lumbar puncture due to the hazard of this procedure in children with posterior fossa tumors. Neurologic and neurosurgical consultation should be obtained soon in these cases as some of the above described lesions can be satisfactorily treated.

DEGENERATIVE DISORDERS

Ataxia associated with the degenerative disorders of the nervous system, as with neoplasms, is usually of gradual onset and tends to be progressive. In some instances the cerebellar dysfunction is combined with spinal cord disease, in other, with cerebral disease.

Friedreich's ataxia is the prototype of the spinocerebellar degenerations. This familial degenerative process was initially described by Friedreich[3] in 1863. The mode of transmission has not been established and may vary in different families. Either sex may be affected. The age of onset is usually under 20 with many cases appearing even under 10 years of age. Ataxia of gait is the usual initial symptom. Characteristically, the disturbance of balance or coordination develops so insidiously that a definite date of onset cannot be given by the family. The child shows a progressive tendency to fall frequently, to stagger on walking, and to meet difficulty in engaging in games with other children. With progression of the disorder, the hands become clumsy and deterioration of handwriting ability is noted by the schoolteacher. Speech becomes dysarthric and eventually indistinct. Early in the disorder, the characteristic foot deformity occurs with a tendency toward plantar flexion, high-arch formation, and marked flexion deformity of the toes. Additional signs found on neurologic examination include hypotonia in upper and lower extremities with diffuse hypo- or areflexia. Position and vibratory sensation are lost in the extremities, although superficial sensory modalities remain intact. The plantar reflexes are variable but later in the course of the disease become extensor bilaterally. A thoracic kyphoscoliosis develops and shows progressive change, as do the other findings. In addition to articulatory speech abnormalities, nystagmus and occasional oscillating head movements may appear. As indicated earlier, ataxia involving both trunkal and appendicular structures is the primary disabling aspect of the early part of Friedreich's ataxia. This has two components as both the posterior columns and the cerebellum suffer in this disease. In the terminal stages of the disorder, optic atrophy and progressive dementia add to the patient's enfeeblement. The pathology is widespread in the nervous system. In the spinal cord degeneration occurs in the posterior columns, the spinocerebellar tracts, and the corticospinal tracts. Fibrillary gliosis replaces the atrophic fibers in these areas. Changes also occur in the brainstem and the cerebellum. The heart shares in the pathologic change in Friedreich's ataxia, and abnormal cardiac findings are often present during the lives of these patients.[4] Cardiac failure accounts for death in some cases. Different types of cardiac pathology have been described, including the findings of chronic interstitial myocarditis,[5] and obliterative coronary artery disease.[6] Using Friedreich's ataxia as a model, it can be pointed out that there are numerous other types of degenerative spinal and spinocerebellar disorders with ataxia as the cardinal clinical manifestation. Hereditary areflexia dystasia (Roussy-Lévy), posterior column ataxia (Biemond), hereditary spastic ataxia, and many others are described by Greenfield.[7] An additional disorder placed in the same general category is referred to as the Marinesco-Sjögren syndrome which is comprised of hereditary cerebellar ataxia, cataracts, and mental retardation.

Among the leukodystrophies, or cerebral white matter degenerative disorders, there are two that are commonly associated with, and frequently initiated by, ataxia. The infantile type of metachromatic leukodystrophy appears between ages 1 and 3 years, with deterioration of gait being the outstanding initial complaint. Following ataxia, progressive spasticity incapacitates the child. In some cases, peripheral nerve involvement supervenes resulting in hypotonia and loss of reflexes. In these cases peripheral nerve (sural nerve) biopsy revealing metachromatic substances will establish the diagnosis. Progressive dementia, nystagmus, and optic atrophy lead to death in these children. A case of metachromatic leukodystrophy with a "cherry red spot" in the retina has been described.[8] Laboratory features of this disorder include an increased spinal fluid protein in the majority of cases. As in the degenerated white matter, the metachromatic ma-

terial accumulates in other organs such as gallbladder, liver, and kidneys. The latter may permit clinical diagnosis if metachromatic granules can be visualized in urine sediment with appropriate stains, such as toluidine blue. Austin[9] has demonstrated these metachromatic substances to be sulfatides (sulfuric acid esters of cerebrosides), thus placing this disorder more closely related to the lipidoses than to the leukodystrophies. This information provides an additional diagnostic approach. Finding an elevated level of sulfatides in the urine virtually establishes the existence of this disease. The clinical course is progressive, sometimes rapidly so, with death occurring within a few months to a few years.

Pelizaeus-Merzbacher disease is another form of white matter dysfunction with ataxia as an early feature.[10] This disorder is a much more chronic process than above and appears to be inherited as a sex-linked recessive trait. Abnormalities are apparent early in infancy with aimless, wandering eye movements, followed by delayed head control and general developmental delay. These infants have often been referred to as "head nodders" by the parents, but with passage of years the neurologic defects become more generalized and advanced. Many live to adulthood but become totally disabled and expire. Recent investigation[11] has revealed almost total absence of stainable myelin in the brain in this disease with the postulate that the basic disorder is a defect in myelin formation rather than in myelin destruction.

The last of the degenerative disorders to be considered is referred to as ataxia-telangiectasia. Mme. Louis-Bar,[12] in 1941, first described the association of cerebellar ataxia with conjunctival and cutaneous telangiectasia. More general awareness of the disorder, however, followed the report by Boder and Sedgwick, in 1957.[13] The primary components of the syndrome include a familial tendency, progressive cerebellar ataxia, oculocutaneous telangiectasia, and recurrent sinus and pulmonary infections. The explanation for the sinopulmonary infections has not become totally apparent; however, some cases have been accompanied by hypogammaglobulinemia.[14] The ataxia usually becomes evident in late infancy or early childhood. Variation exists in this respect as Paine[15] has reported a case with ataxia developing at age 10. Associated findings include reflex loss, abnormal eye movements, drooling, and dysarthria. Telangiectasia usually appears later than the cerebellar ataxia and is first noted in the bulbar conjunctiva, and later upon the butterfly area of the face and external ears. After a few years the ocular telangiectasia may progress to resemble conjunctivitis. While retardation of physical growth becomes gradually apparent, mental faculties remain intact. Death from pulmonary disease is not unusual.

ACUTE CEREBELLAR ATAXIA OF CHILDHOOD

Despite its recognition years ago, the etiology of this syndrome remains unclear. The disorder may occur a few days subsequent to a mild nonspecific febrile illness or it may appear suddenly and spontaneously in a previously asymptomatic child. There is no absolute age limit but between 2-to-5 years seems most prevalent. The child rather abruptly is found to be ataxic, the degree being quite variable. Associated signs in addition to trunkal and gait ataxia may include vomiting and irritability in the early phase of the disorder. Tremor on attempted use of the hands may be apparent in more severe cases and nystagmus may be present. Despite the diagnostic term "acute cerebellar ataxia" some will have mild degrees of hyperreflexia, stupor, or even convulsions. These latter manifestations indicate a process more widespread than simply cerebellar. However, as ataxia remains the outstanding feature this diagnostic terminology would seem the best currently available. Spinal fluid examination usually reveals no striking abnormalities, although a mild lymphocytic pleocytosis has been described. Recovery is likely to occur spontaneously anytime from a few weeks after onset to several months. In one series[16] of 18 cases, complete recovery within six months occurred in 10 patients. Six of the 10 had become asymptomatic within three weeks of onset of the disease. A few of the patients showed persistent cerebellar deficits after prolonged follow-up. Although usually benign, the disease is not invariably so.

The acute cerebellar ataxia syndrome as outlined above is to be differentiated from the ataxic states that occur subsequent to the exanthematous infectious diseases of childhood. Cerebellar ataxia may develop as a complication of chicken pox, measles, mumps, or other common childhood infections. A lymphocytic pleocytosis in the spinal fluid is usually found in these instances. Rarely, cerebellar ataxia has occurred in the preeruptive phase of varicella.[17] Even polio virus infections[18] have been associated with cerebellar ataxic states in children.

METABOLIC DISORDERS

Ataxia as a primary or prominent aspect of the inborn errors or metabolic disorders is unusual. Disturbances of gait not infrequently occur with phenylketonuria; however, here it usually is as-

sociated with mental retardation and abnormalities of tone, including spasticity. The 2 metabolic variants described below are extremely rare diseases but have ataxia as an outstanding feature of the clinical picture.

Hartnup disease was first described in 1956 in England.[19] The patient was a 12-year-old boy with the family name of Hartnup. His family believed he had pellagra because of a scaly, erythematous rash. This rash was especially prominent over the exposed areas of his body. Transient, recurrent, cerebellar ataxia had been part of the past history. The initial report included the detection of a renal amino-aciduria. The clinical features of this inborn error are of interest, in part due to its intermittency. In addition to the skin eruption, episodes of severe but usually reversible ataxia occurred. Apparently this often appears simultaneously with the rash. Both gait and appendicular ataxia is found, and nystagmus is apt to be present in these cases. After several weeks, improvement may result. Emotional lability, confusion, or delirium may accompany the above. In addition to a massive amino-aciduria, abnormal quantities of indican are found in the urine. The absolute definition of the metabolic block is not yet available; however, a disturbance of tryptophan metabolism appears to be present. The few cases reported have shown a familial tendency.

Equally as rare as Hartnup disease is the Bassen-Kornzweig syndrome, described in 1950.[20] This disorder superficially resembles Friedreich's ataxia. However, differences in certain laboratory and metabolic abnormalities have been found. The age of onset of the neurologic abnormalities may be at any time in the pediatric age group, usually later than 2 years. Ataxia, dysarthria, kyphoscoliosis, and proprioceptive deficits are usually found. Pigmentary degeneration of the retina is commonly present. Peripheral blood examination reveals acanthocytosis or a peculiar thorny appearance to many of the erythrocytes. The defects in lipid metabolism include the very low serum cholesterol level and a deficiency of serum beta-lipoprotein.[21] Impaired intestinal absorption of fats may result in steatorrhea. The disorder appears to be hereditary, but as yet the mode of inheritance remains unclear. Despite its rarity, the Bassen-Kornzweig syndrome becomes an important entity as it is a variety of hereditary ataxia with a suggestion of a metabolic defect.

SUMMARY

This review outlines and describes many of the neurologic disorders of childhood manifested by ataxia, but is not meant to be complete. No mention has been made of the cerebellar malformations, for example, which produce neurologic deficits in the very young. In the older child hysteria also can be added in the differential diagnosis, but acceptance of this diagnosis must be left until all possible organic explanations have been excluded.

The mode of appearance, whether gradual or acute, and the subsequent course, whether static or progressive, aid the physician in placing the ataxic disorder in its proper diagnostic category. The associated signs on neurologic examination assist in topographical localization of the lesion in the nervous system. When the answer is not apparent on the initial evaluation, periodic examinations at frequent intervals and appropriate ancillary studies usually eventually provide a solution.

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Genetic Aspects of Achondroplasia

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ACHONDROPLASIA, a rare disease in the general population, occurs with greater frequency among newborns. Its incidence per 1 million people was found to be 15 in the United States,[1] 23 in Denmark,[2] and 28 in northern Ireland.[3] In newborns the incidence varies between 49 and 329 according to the data collected in different obstetric departments in Australia, China, Denmark, northern Ireland, Sweden, and the U.S.[1,4–8] A high perinatal mortality ranging between 75 and 90% accounts for this difference. Considering the low incidence of achondroplasia, its occurrence in both twins must be extremely rare. Rough estimates indicate it occurs not more than once among 1 to 2 million newborns and is even rarer in the general population. We had the occasion to study monozygotic twins with achondroplasia in our clinic. Two newborns with achondroplasia were observed simultaneously. It is the purpose of this paper to present these cases and to review briefly the genetics of achondroplasia.

Case 1. A male was the product of the first pregnancy of a 19-year-old woman of normal proportions with a height of 158 cm. and a weight of 54 kg. The father of the child was an achondroplastic dwarf with a height of 135 cm. and a body weight of 52 kg. The father's parents and his 5 brothers and 3 sisters are all normal. No case of dwarfism is known throughout the family.

The early course of pregnancy was uncomplicated. In later months the mother was slightly hypertensive. The delivery, a vertex presentation, occurred at the end of the thirty-eighth week of pregnancy. The child was born with a birth weight of 2,720 gm., a body length of 43 cm., and a head circumference of 35 cm. The biacromial circumference was 34 cm. A disproportionate dwarfism with very short extremities was noted at birth. The skin over the extremities revealed additional folds. There was considerable muscular hypotonia. The internal organs were normal. Skeletal X-rays were characteristic for achondroplasia.

At three months the child had a weight of 5,040 gm. and a height of 55 cm. The frontooccipital head and the chest circumferences were 42 and 37 cm., respectively. Physical findings except for shortness of the extremities were within normal limits. Skeletal X-rays confirmed the diagnosis of achondroplasia in father and child.

Case 2. A male was the product of the fifth pregnancy of a 23-year-old woman. The family history is not revealing. Other cases of dwarfism or achondroplasia were not known in the family of either parent. The product of the mother's first pregnancy was a 1,400-gm. premature infant who died twelve hours after birth. Three other pregnancies ended in abortions.

The duration of the fifth pregnancy was unknown. An unusual increase of the mother's abdominal circumference was noted during the last month of pregnancy, and hydramnios was found during delivery. The child was delivered by breech extraction. The newborn was breathing irregularly and revealed some cyanosis. Apgar ratings after one minute and five minutes were 6 and 10, respectively. The baby weighed 2,320 gm. and had a total body length of 36.5 cm., with a sitting height of 29 cm. and head and chest circumferences of 35.5 cm. and 27 cm., respectively. The anterior fontanel was wide open and measured 5 × 5 cm. The extremities were extremely short and thickened. Fingers and toes were particularly small, short, and stumpy. No obvious abnormalities of the internal organs were found. Eight hours after birth the child went into respiratory distress and died at the age of 29 hours. An X-ray of the total body was taken postmortem and was consistent with the clinical diagnosis of achondroplasia (Fig. 1). A postmortem examination was done and confirmed the findings of disproportionate dwarfism with a rather long trunk and short, stumpy extremities.

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Fig. 1. X-ray of case 2. Radiological alterations typical for achondroplasia. Height of vertebral bodies decreased. Intervertebral disks 2 to 3 times higher than vertebral bodies. Pedicles of vertebral arches not clearly shown; however, normal increment of interpeduncular distances in lumbar area appears reduced. Ribs are slender. Their bony vertebral end is somewhat irregular. Clavicles relatively long. Scapulas placed more laterally than usual (may be due to smallness of thorax). Long bones short. Diaphyses somewhat thickened; some curved. Irregular epiphyseal lines. Metacarpal and phalangeal bones very short and show irregular epiphyseal lines. Pelvis shows relatively wide iliac wings. Acetabular roof flat, producing very small acetabular angle. Greater sciatic notch shows considerable narrowing. Pubic and ischial bones short and stubby. Iliopubic synchondrosis considerably widened.

The calvarium was bulging in the frontal and parietal area, and the base of the skull was shortened with small fossae. The posterior fossa was particularly small. The occipital foramen was extremely narrow. The brain weighed 305 gm. and was partly autolysed. The thoracic cavity was small, and the heart was normal. The lungs were hypoplastic and poorly aerated. The abdominal organs did not show any abnormalities. The macroscopic and microscopic examinations of the skeleton revealed alterations typical for achondroplasia. The final diagnoses of the pathologist were: prematurity, achondroplasia, small thoracic cavity with pulmonary hypoplasia, partial atelectasis, and compression of the brainstem in consequence of the smallness of the posterior cranial fossa and of the occipital foramen.

Cases 3 and 4. Two female twins with achondroplasia were born on February 3, 1961, as the products of the mother's fourth pregnancy. At that time the father was 32 and the mother was 30 years old. They have 2 normal boys, 1 five years older and the other two years younger than the twins. The mother had had 2 abortions. No other case of dwarfism or achondroplasia is known in the family.

The prenatal history reveals that the mother had a mild depression during early pregnancy and received tranquilizers. She had pneumonia in the fifth month, hypotension and fainting spells during the sixth month, and some edema and anemia during the last month of pregnancy. She gained 53 lb. during pregnancy and polyhydramnios was observed. The delivery was three weeks after the expected term. Both children were delivered spontaneously by breech. The birth weight of twin 1 was 1,950 gm. and of twin 2 1,960 gm. Both twins were kept in an

TABLE 1

DEVELOPMENTAL DATA OF IDENTICAL ACHONDROPLASTIC TWINS

Action	*Age (months)*	
	Case 3 Twin 1	*Case 4 Twin 2*
Rolled over	5	12
Ate by self	11	18
Stood unsupported	18	24
Walked unsupported	20	24
First tooth	12	12
Spoke single words	24	24
Spoke sentences	30	30
Toilet trained	29-32	29-32

TABLE 2

MEASUREMENTS AND PROPORTIONS OF IDENTICAL ACHONDROPLASTIC TWINS AT AGE 32 MONTHS

	Case 3 Twin 1	*Case 4 Twin 2*	*Normal values for age group 2 to 3 years*
Weight	9,900 gm.	9,900 gm.	
Height	73 cm.	78 cm.	
Sitting height	52 cm.	55 cm.	
Sitting height in % of height	71.2%	70.5%	59 ± 1.4%
Frontooccipital head circumference	50.5 cm.	50 cm.	
Frontosuboccipital diameter	13 cm.	12.5 cm.	
Biparietal diameter	14 cm.	14 cm.	
Armspan	64 cm.	68.cm.	
Armspan in % of height	87.2%	87.7%	98%
Hand length (distal wrist line to tip of middle finger)	8 cm.	8 cm.	
Hand length in % of height	10.9%	10.5%	13.2-14.5%

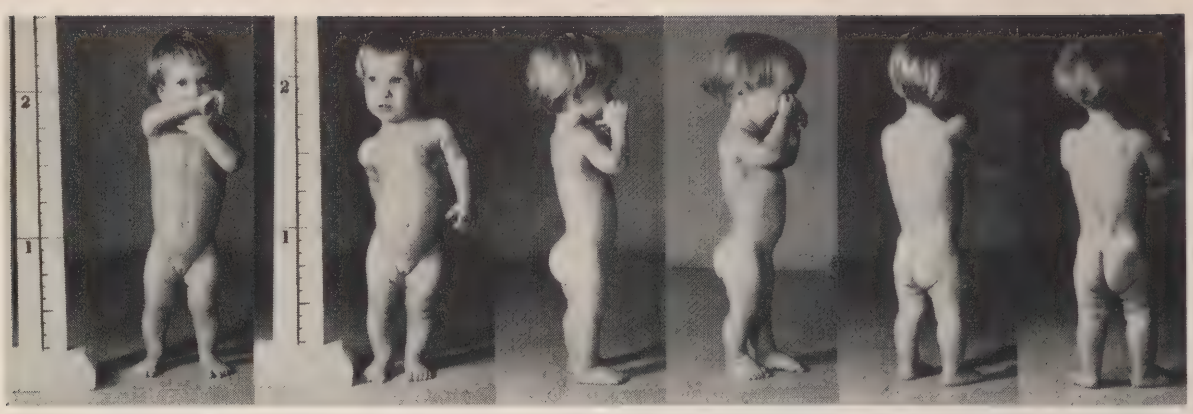


Fig. 2. Case 3 (right) and case 4 (left), identical twins with achondroplasia

incubator for two and a half weeks. Twin 1 is a well behaved, psychologically well balanced girl of apparently normal intelligence. Twin 2 is somewhat slower. She is quite nervous and has frequent temper tantrums. She had a hyperpyrexia of 108° F. (42.3° C.) at the onset of roseola infantum. Ever since, she has shown a tendency to bouts of high fever.

Both twins were examined in the State University of Iowa Hospital when they were 29 months and 32 months old (Fig. 2). On physical examination both had typical signs of achondroplasia: a proportionately long trunk, protruding forehead, sunken bridge of the nose, and shortened upper and lower extremities (see measurements and proportions on table 2). The corneas were clear. No macroglossia, kyphosis, or limitation of joint mobility was noted. Teeth and gingivae were normal. Both twins exhibited moderate muscular hypotonia. Liver and spleen were not felt. The remainder of the physical examination was essentially within normal limits for both.

Routine blood counts were normal in both children. No Reilly granules were found in the leukocytes. Urine examinations were normal, and ferric chloride tests were negative. Urinary mucopolysaccharide excretion (toluidine test) was within normal limits.

Radiological examinations were as follows: There was definite shortening of the base of the skull with a slightly widened sella turcica. The spheno-occipital synchondrosis was not seen. The membranous bones of the skull were normally developed. The inferior branch of the mandible as well as the maxilla was rather small. X-rays of the thorax revealed normal thickness of the ribs and somewhat elongated clavicles. The scapulae did not show any major malformations. The distance between them was relatively increased. The dorsal and lumbosacral spine revealed a moderate overgrowth of the cartilaginous disks. The normal increment of the interpedicular distance in the lumbar area was reduced; the pedicles were rather short. There was some scalloping of the posterior surface of the vertebral body. The anterior surface of the lumbar vertebral bodies revealed a suggestion of a bullet nose deformity (Fig. 3). The iliac wings were rather small and had an almost rectangular appearance. The greater sciatic notches were small and narrow. The pubic and ischial bones were relatively large (Fig. 4). The tubular bones were shortened and revealed some evidence of bowing and widening of the diaphyses. The metaphyses and epiphyseal lines were irregular.

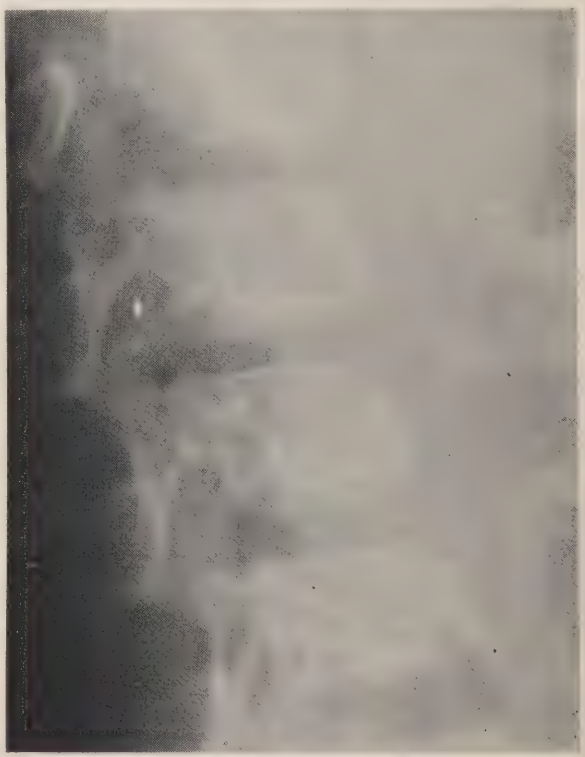


Fig. 3. Lumbar spine of case 3

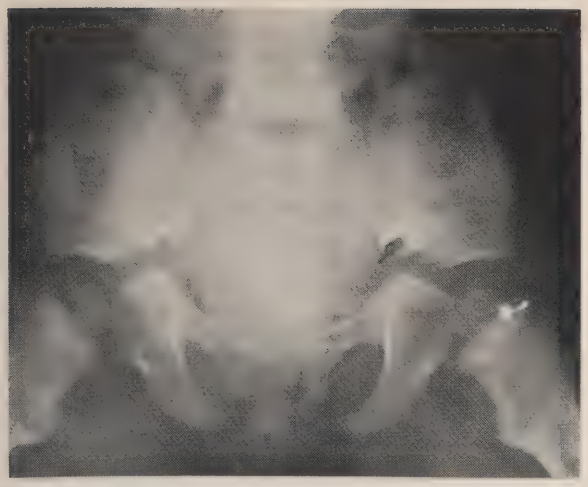


Fig. 4. Pelvis of case 3 at 32 months of age. Discrepancy between small iliac wing and rather large pubic and ischial bones noticeable. Arrow indicates greater sciatic notch; much narrower than in normal controls.

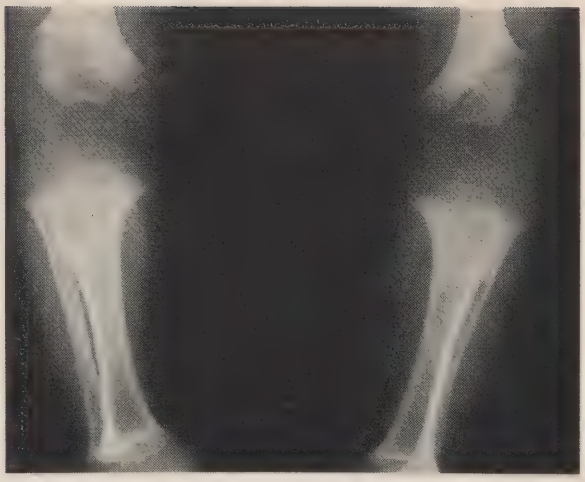


Fig. 5. Knees of case 4 illustrating widened and irregular epiphyseal lines and characteristic indentation of their middle parts by epiphyses, which are of irregular form as well

Some indentation of the metaphyses by the epiphyses was seen in some bones (Fig. 5). Metacarpal, metatarsal, and phalangeal bones were short and stumpy. The bone age was about 1½ years. The X-rays of the twins were almost identical (Figs. 6A and B).

The electroencephalograms were within normal limits for the age of the twins and showed an almost identical pattern. Minor bioccipital sharp activity during wakefulness was present in both records. This is an unusual pattern, perhaps related to visual stimuli.

Chromosomal analysis of twin 1 revealed a normal complement of 46 chromosomes with an XX sex chromosomal constitution in 29 plates. One plate had 45 chromosomes, with one C chromosome missing. One plate revealed a small fragment. Twin 2 had a normal complement of 46 chromosomes with an XX sex chromosomal constitution in 19 plates. Two plates had 45 chromosomes, with one E chromosome missing in both cells. In one, a small fragment was seen. One tetraploid karyotype was found with 96 chromosomes and 1 small fragment. Another one had 98 chromosomes, including 2 supernumerary F chromosomes plus 2 small fragments.

Both twins had identical hair and iris color.



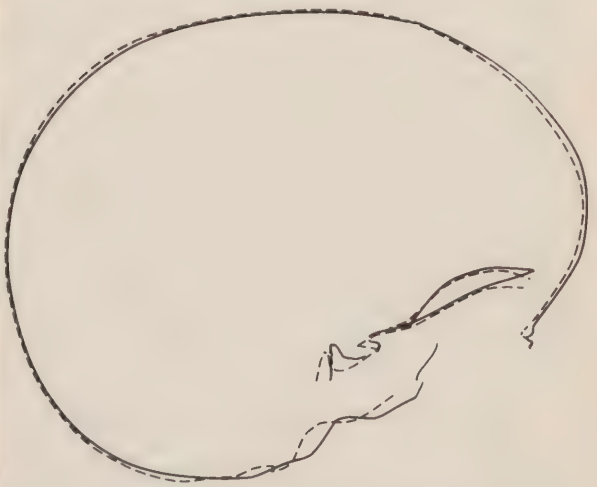


Fig. 6A. *(left)* Left arm of case 3 (left) and of case 4 (right); almost complete congruence of size, form, and maturation. Fig. 6B. *(right)* Contours of outer plate of skull of case 3 (broken line) and case 4 (full line); considerable, although not complete, congruence

TABLE 3

A. BLOOD GROUPS OF PARENTS AND CASE 3 (Twin 1) AND CASE 4 (Twin 2)

	ABO	*Rhesus*	*MN*	*Kell*	*Fya*	*Lea**
Father	B	CDE/cde	M+N+	K—k+	+	+
Mother	B	CDe/cde	M+N—	K—k+	+	—
Case 3, Twin 1	B	CDe/Cde	M+N+	K—k+	+	+
Case 4, Twin 2	B	CDe/Cde	M+N+	K—k+	+	—

B. ANALYSIS OF Lea FACTOR IN CASES 3 AND 4

	Serum dade†	*Hyland*	*Ortho (Usable for trypsinized cells)‡*
Case 3, Twin 1	±	—	—
Case 4, Twin 2	—	—	—

*Tested with orthoserum not usable for trypsinized cells. This is a potent serum with high antibody concentration, yet it is less specific than the orthoserum used in subsequent tests.

†Case 3 yielded an equivocal reaction with Dade serum which was interpreted as a nonspecific reaction.

‡Orthoserum used for this test is less potent yet more specific than orthoserum used in the first test (Table 3A).

Six different blood groups of the parents and both twins were determined. Results are presented in table 3. The twins were concordant in the ABO, MN, Rhesus, Kell, and Duffy systems. The Lewis[a] factor was negative in twin 1 and positive in twin 2 on two occasions when examined with a potent but less specific orthoserum. Several months later the blood was examined, with 3 more specific Lewis[a] test sera. The results are shown in table 3B.

A mutual skin graft from Twin 1 to twin 2 and vice versa healed without complication.

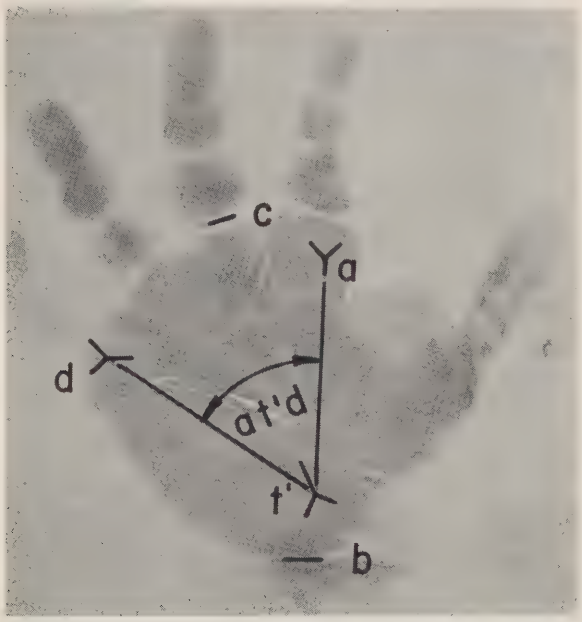


Fig. 7. Palm print of case 3. t′ indicates proximal triradius; b, distal wrist line; and c, metacarpodigital line of middle finger. Ratio of $\frac{b\ t'}{b\ c}$ almost identical in both twins

Palm prints were taken of both twins and revealed a proximal triradius (t′) in both. The ratio between the distance from the distal wrist line b to t′ to the distance between the distal wrist line and the metacarpophalangeal line of the middle finger was almost the same for both. The at′d angle was between 50 and 60° in both hands of either twin (Fig. 7). The fingerprints were difficult to establish. Ridge counts could not be made. Good prints were obtained of only 4 comparable fingers of either twin. They all showed an ulnar loop pattern which was identical for corresponding fingers of both.

DISCUSSION

The 4 cases presented are typical examples of achondroplasia. Case 1 was a sporadic case, case 2 was a child with an achondroplastic father, and cases 3 and 4 were twins from a family in which there were no other cases of achondroplasia. Achondroplasia—the term was introduced by Parrot[9] in 1878—has also been called fetal rickets, fetal chondritis, fetal sclerosis, micromelia, chondromalacia, fetal chondrodystrophy, and fetal chondrodysplasia. The frequent use of the adjective "fetal" in these different terms indicates the prenatal origin of this condition.

Environmental factors acting during early pregnancy as well as genetic factors have been considered as causes of achondroplasia in men and animals and shall be discussed briefly. Environmental factors have been found to produce achondroplasia in birds and lower mammals. Eserine, sulfa, radioactive sulfur, thallium, and insulin administered during the early fetal period can produce animals with an achondroplasia-like condition.[10,11] The production of

human achondroplasia by chemicals and drugs has, hitherto, not been reported; yet endocrine disturbances of the thyroid,[12] parathyroids,[13] and gonads,[14] plus intrauterine infections, intoxications,[27] and parental alcoholism have been incriminated at times. Alterations of the amnion sac, oligohydramnios, as well as polyhydramnios were mentioned among the causes of human achondroplasia.[2,3,17–19] Incidentally, hydramnios was found in the mothers of the infant of case 2 and the twins. How hydramnios could cause achondroplasia is difficult to conceive. Hydramnios is found to be associated with many different malformations. One may conjecture, therefore, that hydramnios is a concomitant manifestation of the malformation rather than its cause. So far, no case of human achondroplasia has been reported where an environmental factor could definitely be held responsible for its causation.

Most of the cases of achondroplasia are not familial but occur as sporadic cases. This, then, would suggest that they are due to mutations, since environmental factors have been excluded as causes of achondroplasia. Mutations, for example, suddenly appearing alterations of the genome, may involve smaller (single gene) or larger (several genes) areas of the DNA strand or the whole DNA strand of a chromosome. Mutations involving a single gene are called point mutations. Mutations involving microscopically recognizable parts of a DNA strand, such as a fragment or a whole chromosome, are called chromosomal aberrations. In the literature available to us, chromosomal aberrations in achondroplasia have not been described. Harnden,[20] Giraud and others,[21] and Haylock and others[22] reported a normal chromosomal complement in achondroplasia. Thus, the finding of several chromosomal aberrations in some cells of either twin, such as loss of a chromosome, presence of an additional fragment, and presence of a few tetraploid cells, came as a surprise. Any one of these aberrations may arise during the different technical procedures necessary for the preparation of the karyograms. The association of several aberrations in the same individuals, as in cases 3 and 4, is most unusual. Moreover, chromosomal studies of 3 other patients done on the same day and with similar techniques did not show any abnormalities. One wonders, therefore, whether the chromosomal aberrations found in either twin could not be of some significance; perhaps they indicate a certain vulnerability inherent in the chromosomes of these 2 patients. Data were presented elsewhere[23] suggesting that the finding of similar or related chromosomal aberrations in a minority of cells may indicate a propensity to other chromosomal aberrations such as trisomy 21. In this connection a pair of twins, one achondroplastic, the other mongoloid, reported by Lapage,[24] may be of interest.

It is generally accepted that the majority of all cases of achondroplasia are due to a point mutation. The mutation rate as indicated by different authors[2,3,25] varies between 1 in 9,000 to 13,500 in terms of individuals or 1 in 18,000 to 27,000 in terms of genes or chromosomes. No mutagens have so far been found with certainty. It appears, however, that the mutation rate increases with increasing maternal[26] or paternal[2,28] age. Fathers over 35 have a mutation rate four times higher and fathers over 40, a mutation rate ten times higher than those below 30 years of age.[29,30] Lenz[30] negates an influence of maternal age on mutation rate, which is in striking contrast to the observations made in mongolism, where the correlation between maternal age and mongolism is well established.[31]

The high infant mortality in combination with the presumptive decreased fertility[32–34] of achondroplastic dwarfs makes the study of the hereditary transmission difficult, since a rather rapid elimination of this mutation can be assumed. According to Fraser-Roberts,[25] there is a strong tendency for this mutation to disappear within a few generations. It is, therefore, not surprising that very few familial cases have been reported. Only a few families have been reported in which achondroplasia occurred in 2 generations, and very few families are known with achondroplastic patients, dwarfs, in 3 generations.[2,28,35]

Transmission from one generation to the next suggests autosomal dominant inheritance of the mutant gene. Approximately 50 observations of achondroplasia of one parent and of several of his or her children are available. The family of case 2 represents an additional example. Cebron[36] reported a case of an achondroplastic mother who had 2 children with achondroplasia, each from a different husband. All these observations suggest an autosomal dominant transmission of the mutant gene.

Grebe[28] observed 2 families in which healthy consanguineous parents had children with achondroplasia. He was inclined to postulate an autosomal recessive pattern of inheritance for these cases. However, Grebe's observation can also be explained if one assumes incomplete penetrance of a dominant gene. Incomplete penetrance of the dominant gene likewise explains the following observations: Chiari[37] described 2 achondroplastic children (half siblings) of a normal father, each born of a different,

normal woman. Several authors[1,3,27,38] observed sibships with 2 or more achondroplastic children born to normal parents. Of course, a point mutation in the precursors of the gonadal cells (stem cells of the ovogonia or spermatogonia) could account for the occurrence of more than one affected child of normal parents. Although recessive inheritance has not been fully excluded,[15] autosomal dominance has been accepted as the prevailing mode of inheritance of achondroplasia. In this connection it is interesting to notice that other bone diseases with a somewhat similar phenotype, for instance Ellis–van Creveld's disease (a combination of achondroplasia with ectodermal dysplasia and congenital heart disease) and Morquio's disease, follow an autosomal recessive pattern of inheritance.

The mode of transmission of achondroplasia in animals varies. Achondroplasia of creeper fowl[39] follows a dominant pattern of inheritance, while recessive inheritance is found in certain forms of canine achondroplasia.[18]

Information concerning the progeny of 2 achondroplastic parents is scanty, although a number of marriages between achondroplastic dwarfs have occurred.[30] Grebe[27] cited Schmidt[40] and Franchini[41] who each reported an achondroplastic child born to achondroplastic parents. Von Meyenburg[42] examined an achondroplastic fetus, product of the mating of 2 achondroplastic dwarfs. Similar observations were made by Mørch[2] and Potter.[4] On the basis of theoretical considerations and in analogy to observations in animals, one could expect that homozygosity of the achondroplasia gene would represent a lethal factor. If this assumption is correct, one would expect that one-fourth of the zygotes produced by achondroplastic (heterozygous) parents would be lethal, while of the remaining offspring two-thirds would be achondroplastic and one-third phenotypically and genotypically normal. Further observations are necessary to prove the validity of this hypothesis.*

Cases 3 and 4 are achondroplastic twin dwarfs. Hence, they are concordant with respect to their bone disease. They have the same color of iris and hair. According to our electroencephalographer (Dr. E. Niedermeyer), the electroencephalograms of both twins are so similar that one record can be considered as a continuation of the other. This is a typical finding in 80% of identical twins. Both twins show certain differences with respect to their phenotypic appearance (Fig. 2), their psychomotor development (Table 2), and their character and behavior. Nevertheless, identity could be established within the range of statistical significance by the concordance in 6 different blood groups, the concordance of their finger and hand prints (as far as these examinations could be performed), and by the successful transplantation of mutual skin grafts. The examination of finger patterns was incomplete due to lack of cooperation of the probands.

Discordance was initially found with respect to the Lewis^a factor. However, Lewis^a positivity is age-dependent[44] and a Lewis^a positive infant may become negative in childhood or later. Moreover, nonspecific antibodies may interfere with the correct determination of the Lewis^a factor. Hence, discordance in the Lewis^a factor would not preclude identity of the twins presented in cases 3 and 4. However, retesting of the twins with several more specific Lewis^a antisera established concordance with respect to this blood group as well.

It was mentioned earlier in this paper how rare twins with achondroplasia ought to be. Nineteen twin pairs, including our observations, have been reported so far, of whom one or both twins were affected with achondroplasia (Table 4). Besides the twin pair presented here, only 2 pairs of identical twin girls concordant for achondroplasia have been described, the cases of Cohn and Weinberg[45] and Pfändler.[50] Presumptive identity was established in the former case by the presence of a single placenta, a single chorion, and the concordance in 3 different blood group systems. In the latter case identity was established by concordance in 3 blood group systems and by a great number of similar physical characteristics such as color and pattern of hair and eyebrows, iris color, or presence of lentigines. Nine pairs of twins of the same sex with achondroplasia have been described; their zygosity was not established with satisfactory exactness. Five of them were concordant with respect to achondroplasia, while only one twin was affected of 4 (same sex) pairs, of which one was monochorionic.[53] Four other twin pairs were of different sex, hence they most probably were dizygotic. Twice both twins were achondroplastic, and twice one twin only was affected. The sex of 3 further pairs discordant for achondroplasia was not recorded.

Since usually about 25% of all twins are monozygotic, one could assume that 5 of the above 19 pairs could be monozygotic (for example,

*One speaks of complete dominance when the heterozygous state cannot be distinguished from the homozygous state and of intermediate dominance, also called incomplete, partial, or semidominance, if the clinical picture of the homozygous is more severe than the heterozygous gene carriers. If future investigation should confirm the observation of the above-mentioned authors, intermediate dominance would represent the mode of inheritance of achondroplasia.

TABLE 4

TWINS AND ACHONDROPLASIA

Key:	*Achondroplasia*	*Normal*
Male	■	□
Female	●	○
Sex unkown	◆	◇

Year	*Author*	*Twins*
Monozygosity established:		
1945	Pfändler[50]	●●
1956	Cohn and Weinberg[45]	●●
1964	Cases 3 and 4	●●
Same sex:		
1906	Chambrelent[46]	●●
1911-12	Schemensky and Lommel[47]	■■
1923	Bernstein[48]	■■
1945	Goodman[49]	●●
1945	Grebe[27]	◆◆
1928	Warner[51]	■□
1933	Lapage[24]	■□
1934	Benjamin[52]	●○
1957	Grassi-Lorenzi[53]*	■□
Different sex:		
1817	Romberg[54]	■●
1885	Dyes[55]	■●
1910	Hutchison[80]	●□
1912	Rieschbieth[56]	●□
Sex unknown:		
1893	Müller[57]	●◇
1901	Klein[58]	◆◇
1938	Peralta[43]	◆◇

*Monochorionic twins

our cases 3 and 4, observations of Cohn and Weinberg,[45] of Pfändler,[50] and 2 other pairs). The 14 remaining pairs would then be dizygotic. Of these, 5 are concordant, and 9 are discordant, with respect to achondroplasia. This ratio corresponds fairly well to the ratio of concordance and discordance among dizygotic twins, provided a single gene mutation follows an autosomal dominant pattern of inheritance.

SUMMARY

Four cases of achondroplasia are presented. One was a familial case with a dominant mode of inheritance. One was a sporadic case, and 2 cases were identical twins. Incidence, mutation rate, genetic aspects, and infant mortality of achondroplasia are discussed with special reference to the cases presented.

We are indebted to Michael R. Liesch, M.T., for the analyses of the blood groups in cases 3 and 4.

Supported by grant B 2543 from the United States Public Health Service, National Institutes of Health.

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STIFF-MAN SYNDROME, characterized by muscular rigidity and associated tonic spasm, probably is caused by impairment of the inhibitory mechanism of the anterior horn cells. A physiological or pathological block occurs in the synaptic junction between the interneuron of the inhibitory pathway and the motor neuron. Muscles of the trunk, neck, abdomen, and back are principally affected, and extremities also may be involved. Spasms are frequently initiated by emotion or such external stimuli as noise. Tight abdominal musculature may restrict food intake to small, frequent amounts, and tight respiratory muscles may cause shallow respiration. Muscle strength appears to be normal, and atrophy does not occur. Sensory perception is not affected. Deep tendon reflexes are active or hyperactive and equal; plantar responses are normal. The basal metabolic rate may be elevated, reducing substances may be present in the urine, and glucose metabolism may be altered. Electromyography reveals persistent and diffuse discharge of normal motor unit potentials. Data are based on a study of 3 patients and a review of 24 reported cases. Administration of 60 mg. of diazepam daily improved 2 of the 3 patients.

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Auditory Reactions of the Neonate

A Preliminary Report

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INTRODUCTION

In 1958, an article by Russian scientists reported that sound of even moderate intensity suppressed sucking movements in the neonate. Bronshtein and associates[1] observed sucking patterns of neonates by a pressure-sensing device attached to a nipple. This device was connected to a kymograph upon which the sucking patterns were recorded. They subjected their infants to a variety of sounds in order to determine if the patterns of sucking changed upon presentation of different auditory stimuli. The majority of infants, quite independent of their age, performed 9 to 12 sucking movements and then stopped. The range varied from less than 5 to more than 18 sucking movements in a series. Approximately one-half of the time interval the infants sucked, whereas during the other half they did not. The index of activity did not depend on the age and was equal in the oldest and youngest infants under investigation. The authors arrived at the following conclusions:

1. The ability to react to sound constitutes an inborn property of the human being.

2. Infants in the first month of life may, to some degree, differentiate between the quality of the stimuli—for example, loudness, direction, and pitch of sound.

3. On repeated presentation of the stimulus, the reaction to it ceases as a rule. The rate of cessation depends on the quality and potency of the stimulus and the condition of the nervous system.

4. In healthy infants, 11.8% stopped sucking on presentation of an auditory stimulus of 60 to 70 decibels only once, 22.8% reacted twice, and 5.5% of the babies continued to react even after 10 or more presentations of the stimulus were made.

5. Newborn infants in whom a trauma had occurred during birth, "and the majority of these cases were infants whose brains were subjected to increased pressure," were also tested. In 4% cessation of sucking occurred after 1 stimulus presentation, but in 30% the infants stopped sucking each time the stimulus was presented.

6. It was emphasized that this continued response could still be elicited after all traces of the "trauma" had disappeared and the infants were considered clinically healthy.

7. Observations similar to those recorded on traumatized babies were also found in hydrocephalic infants and healthy prematures.

In short, the majority of healthy infants stopped responding to a tone stimulus by cessation of sucking after 2 or 3 presentations. On the other hand, traumatized newborn and healthy prematures stopped sucking each time the tone stimulus was presented.

THEORY

The Russian workers used the following theory to explain their results: The cortex is the most vulnerable part of the central nervous system and suffers most in all cases of trauma. Therefore, in infants as well as in animals with a temporarily dissociated cortex, the control over the subcortical areas is lost and the subcortex functions without restraint.

Kaye and Levin[2] attempted to examine the effects of tone presentation on sucking rates. They observed the sucking responses of 2 groups of neonates; 1 group was presented with auditory stimuli (tones) and the other was not. Their results suggested that suppression was not easily demonstrated in the first four days of life and that, although there was an apparent decrement in sucking in the experimental group following

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tone presentation, there were similar changes in the sucking patterns of the control group.

Richmond and associates[3] evolved a hearing test for newborn infants by subjecting them to a percussion type cowbell with an intensity of 113 db. The response was recorded as positive by a palpebral or startle response. All subjects responded; the palpebral response was the most significant, being present in 70%. There was no response when the child was crying or actively nursing. Hardy and associates[4] used a similar technique with newborn infants employing a wooden "clacker" which produces a stimulus with a sharp, short, percussive peak of approximately 60 db. intensity and a frequency range up to 8,000 cps. A Moro or startle response or any part of the Moro response, such as a jerk or an eye blink, was considered satisfactory if it was elicited immediately following the stimulus, 2 out of 3 times, the stimulus being applied approximately at two-minute intervals when the baby was awake. Of 64 infants tested, 55 responded with a complete or partial Moro response; 9 failed to respond accurately and of these, 5 showed other neurological abnormalities. Four of the 64 had normal hearing response but abnormal neurological findings.

Obviously, present methods of evaluation of the newborn as prognostic indicators of future psychomotor development are woefully inadequate. If the Russian results can be replicated, adaptation of neonates to auditory stimuli as observed in their sucking patterns would be a useful tool in determining infants with cerebral dysfunction and an aid in the recognition of "suspicious" babies who could be followed on a longitudinal basis for deviations in growth and development. This procedure used by the Russian workers is a relatively simple and painless one easily acceptable by mothers and takes only a few minutes to accomplish. In view of this, a pilot study was organized and executed.

PILOT STUDY

Subjects. Initially, it was planned to use both 1-day and 3-day-old infants as subjects. However, the former group of infants was very erratic in their sucking performance, and most of those used would not complete the experimental procedure. Consequently, subjects for the pilot study were 10 infants between 48 and 72 hours old with no detectable abnormalities of any type.

Auditory stimuli. Two types of auditory stimuli were used, a 500 cps square wave (stimulus A) and electronically generated pulses of 50 cycles per second (stimulus B). The rationale for the use of these stimuli was as follows:

1. Since the auditory range of newborns with respect to frequency is unknown, a broadband stimulus, such as a square wave, seemed desirable.

2. Pulse stimuli have been shown to arouse the greatest degree of neurophysiological response in psychoacoustic and EEG audiometry research.

After seventeen seconds of silence these stimuli were presented over 3 five-second intervals with one second of silence intervening. This thirty-four-second, rest-stimulus sequence was re-

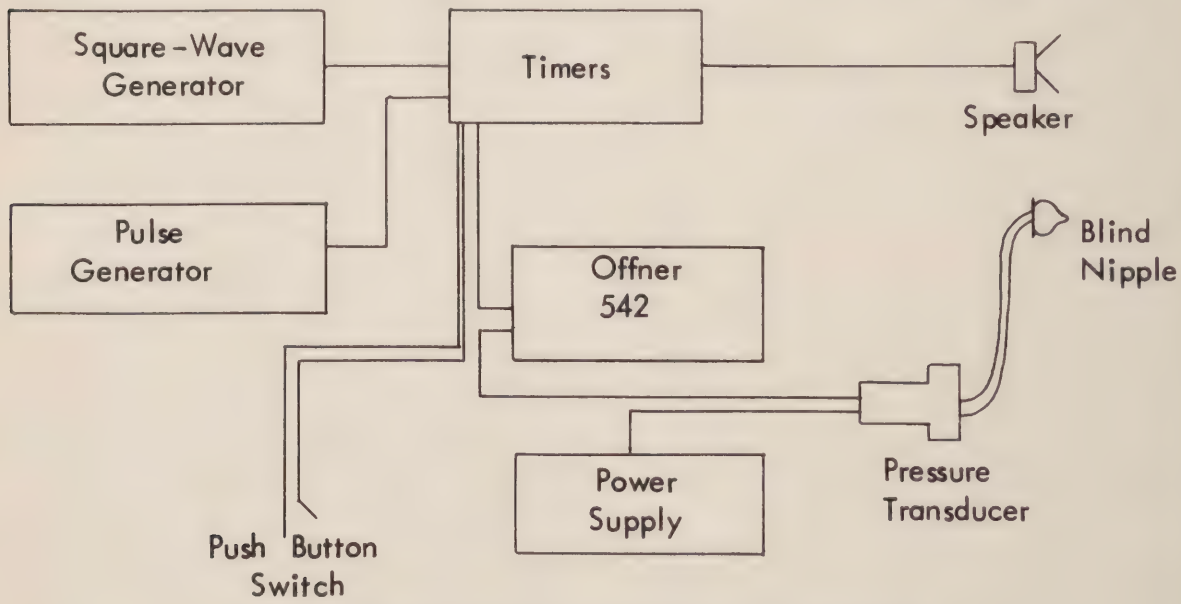


Fig. 1. A block diagram of the equipment used in the pilot study

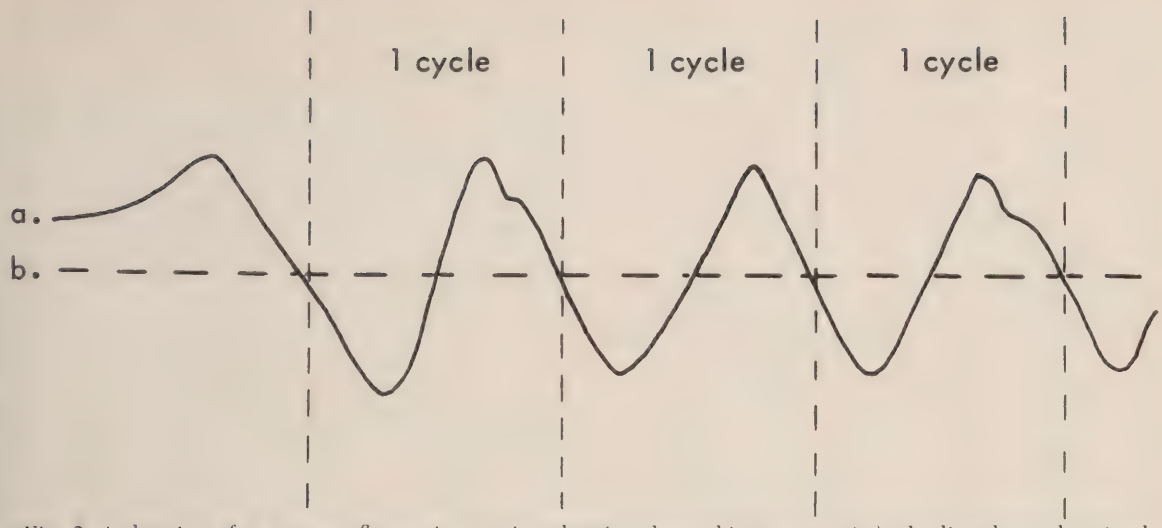


Fig. 2. A drawing of a pressure fluctuation tracing showing the sucking pattern (a), the line drawn by visual inspection through the midrange of that pattern (b), and the delineation of cycles of sucking

peated 10 times for each condition. Both types of stimuli were presented at a level predetermined to be 65 db. at the right ears of the subjects. The intensity level for their left ears was undoubtedly lower, but it was not measured.

The order of the conditions was reversed for 5 of the 10 subjects; for example, the first 5 subjects were presented with square wave (stimulus A) followed by the pulses (stimulus B), and for the remaining 5 subjects the order of conditions was reversed. Therefore, the entire experimental procedure lasted eleven and three-tenths minutes, in addition to a rest period between the 2 conditions.

Equipment. Figure 1 shows a block diagram of the equipment used. The stimuli were generated by the square-wave generator (stimulus A) and pulse generator (stimulus B). One of the experimenters timed the periods of silence and depressed the push button to set the timers into operation. They served to control precisely the five second on, one second off, five second on, one second off, and five second on sequence of the stimuli. The stimuli were presented to the subject by a Jensen D30 speaker, and they were simultaneously recorded on 1 channel of the Offner 542 Dynograph paper writer.

The pressure fluctuations in the blind nipple, created by the sucking of the subjects, were converted to an electrical voltage by a Statham PM 131 pressure transducer. These voltage changes were then recorded on the other channel of the Dynograph.

Experimental conditions and procedures. The subjects were tested just prior to a scheduled morning feeding. They were placed supine in a bassinet. The head was supported in an adjustable device designed to minimize lateral movement of the head. A blind nipple, with a tube attached connecting it to the transducer, was held by an instrument clamp and steel rod above the subject in such a way that it moved in the sagittal plane of the subject. This arrangement permitted considerable movement of the infant's head before the nipple would be forced out of the mouth.

After the infant was placed in the bassinet and the nipple inserted into the mouth, the pressure tracing was observed on the Dynograph until a rhythmic sucking pattern was obtained. One of the experimenters then marked the chart paper to coincide with the beginning of the timing of the first period of silence, and the procedure began.

The room in which the experiment took place was adjacent to the Newborn Nursery, S.U.I. General Hospital. The ambient noise level was judged to be appropriately low. (The reports of Bronshtein and Petrova[5] indicated that low level ambient noise should not be a matter of concern.)

RESULTS

Analysis of the data. The tracings of intranipple pressure fluctuations proved difficult to analyze, since any movement of the lips or jaws of the infants were reflected therein. An arbitrary judgment was made in this regard as follows:

1. A pressure level was visually determined which was judged to be the midpoint of the pressure fluctuations during sucking patterns. A line was drawn on the chart at that level.

2. One cycle of sucking was counted when the pressure trace crossed this line twice. Figure 2 demonstrates this analysis.

TABLE 1
SUCKING RECORD FOR INFANTS

Number of period	A_1	*B*	*D*	A_2	*C*	*D*
1	19.2	16.7	2.5	19.6	14.9	4.7
2	15.5	14.3	1.2	18.4	17.4	1.0
3	15.3	13.5	1.8	15.9	16.3	–0.4
4	16.9	16.8	0.1	14.1	14.9	–0.8
5	15.3	14.4	0.9	18.8	18.0	0.8
6	13.9	14.7	–0.8	17.6	14.1	3.5
7	17.6	17.3	0.3	16.7	17.4	–0.7
8	15.2	16.1	–0.9	19.4	16.2	3.2
9	18.0	14.5	3.5	15.3	17.0	–1.7
10	14.7	15.1	–0.4	17.2	16.6	0.6
Means	16.2	15.3	0.9	17.3	16.3	1.0

The mean number of cycles of sucking recorded for 10 infants during 10 periods of silence (A_1) and associated presentations of a square wave (B), 10 periods of silence (A_2) and associated presentations of a train of pulses (C), and the means of differences (D) between each silence and stimulus presentation

3. The number of complete cycles of sucking for periods of rest and periods of stimuli presentation was tabulated. Table 1 presents these data. The most meaningful comparisons are the differences in the number of cycles between periods of silence and periods of stimuli presentation. The obvious lack of marked differences between the periods of silence and associated periods of stimulus presentation (column D) makes statistical analyses of these data unnecessary. It is unlikely that any of these differences would prove statisically significant.

Discussion. It is to be noted that for the square-wave stimulus (B) the subjects sucked less rapidly during the stimulus presentation than the associated period of silence for the first 5 silence-stimulus periods. For the train of pulses, this situation was true for only the first 2 silence-stimulus periods. These trends might suggest that the conclusions of the Russian writers were confirmed to some extent by these data. Yet, note that, for period number 9 for the square-wave presentations (B) and for periods number 6 and 8 for the pulse train stimulus (C), the differences were of similar magnitude (or greater) than during the first period for both stimuli.

To have corroborated the conclusions of the Russian workers, our data should have shown the following trends:

1. There should have been a substantial difference between the first period of silence and the associated period of stimulus presentation.

2. This difference should have decreased with successive silence-stimulus presentations, and the neonate subjects should not have reacted to the stimuli once this difference was eliminated.

Moreover, perusal of the data indicates that only 3 of the 10 neonate subjects of the present study ceased their sucking activity during any 1 stimulus period. This cessation was during the first stimulus for 1 infant, and second, third, fourth, eighth, ninth, and tenth periods for the third infant. These periods of cessation were not consistent for the 2 types of stimuli, and these 3 infants also ceased their sucking activity during some periods of silence.

TENTATIVE CONCLUSIONS AND IMPLICATIONS FOR FURTHER RESEARCH

A tentative conclusion might be that the results of this pilot study, in combination with the results of Kaye and Levin, in no way support the Russian research. However, such a conclusion might be premature.

The work of the Russians, as can be determined by their reports, seems quite unsystematic. Insofar as possible, the present study was designed to replicate their procedures with 1 exception. The communication of Bronshtein and Petrova states that between presentations of stimuli (five seconds on, one second off, five seconds on, one second off, and five seconds on) "we observed pauses of one to two minutes." It is not clear whether their infant subjects continued sucking throughout their study. Our assumption was that such a prolonged procedure (a minimum of fifteen minutes with one-minute periods of silence) would have introduced periods of fatigue. Therefore, in the present study, the silence periods were reduced to equal those of the stimulus periods.

The assumption regarding fatigue was shown to be false. Perusal of the data suggested no demonstrable effect upon sucking patterns of the present subjects by the eleven and three-tenths minute procedure. The 15 neonates who did not complete the procedure were usually erratic in their sucking behavior before beginning the procedure and continued to be erratic throughout attempts to use them as subjects.

Also, and probably of greater importance, the data of the present study suggest that the relatively rapid silence-stimulus sequence may have had an interaction effect upon the sucking behavior of the 3-day-old neonates. Table 1 shows a relatively consistent decrease in the mean cycles of sucking throughout the first 3 silence periods and stimulus periods (a decrement of from 19.2 to 13.5 cycles). Subsequently, the mean cycles of sucking per period again increased and did not drop to the 13.5 level. If this trend does represent a reaction to the stimuli and if the increase does represent an adaptation effect upon

the subjects, the present data may well indicate justification for further research.

This research should probably take the form of systematically changing types of stimuli (the train of pulses obviously had less effect upon the present subjects than the square wave), intensity of stimuli, and temporal sequence of silence-stimulus periods. Also, subsequent study should use control groups, and both the experimental groups and control groups of neonates should be relatively large in number to insure that population variability may be accurately detected by statistical procedures.

If, by the procedures described above, a method can be devised whereby reaction of neonates to auditory stimuli can be reliably determined, the potential of this work should be obvious. Not only might it provide early detection of central nervous system abnormality, as suggested by the Russian authors, but, if combined with appropriate longitudinal observations, it could conceivably provide a clinical tool for detecting congenital hearing loss in newborns. Therefore, this line of research is being pursued.

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REGULAR INSULIN in multiple daily doses more effectively controls brittle diabetes than single doses of a long-acting drug. Brittle diabetes with its extreme, unpredictable lability of glucose metabolism, does not respond to antidiabetic measures in ketosis-prone, insulin-deficient, and insulin-sensitive patients with wide fluctuations of hypo- and hyperglycemia. Hyperlability probably is due to dysfunction of plasma-protein transport and hepatic and peripheral tissue metabolism which results in irregular hormone inactivation and reactivation. Recommended management includes administration of unmodified insulin 3 times a day with feedings every five hours, and a fourth feeding and administration of semilente insulin before the nine-hour night period. The frequency of depression in patients with long-standing brittle diabetes must be considered in planning therapy.

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EXTENSIVE ASCITES without acute peritonitis may be due to escape of bile into the peritoneal cavity. Usual situations leading to the condition are accidental severance of the bile ducts during operation or slow leakage from an operative site in the biliary tract. The former defect is repaired surgically and the latter treated by paracentesis. The benign nature of the illness may be explained by the slow rate of leakage and lack of major bacterial contamination of the bile. Patients have abdominal distension without marked abdominal pain, fever, or leukocytosis. They may have jaundice, anorexia, nausea, acholic stools, and diarrhea.

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An Objective Study of Psychological Factors in Ulcerative Colitis in Children

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Although the etiology of ulcerative colitis is controversial, the 3 different factors of infection, allergy, and psychological conditions are considered the main pathogenic possibilities. Probably more has been written about the psychological factors than any other point of view, and many investigators emphasize the importance of them in the disease.[1,2,3]

Study of the disease in children provides an important opportunity for better understanding since most present day explanations maintaining the importance of psychogenic factors in adults emphasize the significance of childhood experience. Sperling[4] believes that the disease even in adults actually originates in childhood and that clinical manifestations remain latent until adulthood is reached.

While many writers emphasize the importance of psychological factors, many also do not wish to exclude the possibility of other factors being of greater consequence. For example, some favor the view that the disease is due to an infectious agent and some believe that it is some type of collagen disease. Viewpoints other than a psychological one are effectively presented by Levine and associates,[5] Hauch,[6] and Rowe and Rowe.[7] The allergy viewpoint exemplified by Rowe and Rowe has fewer adherents. Mohr's[8] views are representative of the position of those investigators who maintain that the psychological aspects of ulcerative colitis are predominant. He sees the disease entity as consisting of (1) some "predisposing factor," (2) the presence in the child's life of some "conflict situation," and (3) the existence of some "precipitating event." Finch and Hess,[9] although identifying with the "psychogenic" viewpoint, believe that the psychological factors are not easily explained or delineated. They studied 17 children with the disease, ranging in age from 4 to 14 years, using case histories, psychiatric evaluations, and the Rorschach, Thematic Apperception, figure drawing, and sentence completion tests. The data are reported in subjective and nonquantifiable forms, but the study, however, supports the observations of clinical investigators. Finch and Hess do not believe that their study contributed to an understanding of etiology, and neither do they think they found a direct relationship between psychological disturbance and disease symptomatology. Their conclusion that no specific or unique factors were found in the development of the children studied supports the similar and earlier view of Weinstock.[10] They suggest the disease has a broad "base" and individual characteristics must be taken into account with no single type of treatment being generally effective. They do maintain, nevertheless, that all children with the disease have some severe form of psychopathology. These investigators, as do many others, feel that the family situation has much significance in understanding the psychopathology of the child.[11]

Although considerable agreement is found in the view that psychological factors are of consequence in the disease, objective evidence that can be quantified or obtained by other investigators is generally lacking. Engel,[12] who has written extensively about ulcerative colitis, believes the same approach should be used for ulcerative colitis as was used for malaria. That is, there should first be a description of what is found, so that from this information objective and scientific knowledge can be organized. Accordingly, an essential requirement for increased understanding is a quantifiable assessment of psychological characteristics encountered in the disease process. Resolution of different viewpoints accounting for the disease can be achieved only by data which are minimally dependent upon subjective evaluation.

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Fig. 1. Drawings of the 5 stimulus cards used in the present study. The original cards are black-and-white photographs.

Two steps are needed for a beginning: (1) a theoretical approach sufficiently delineated so that testing of a basic framework of explanation can be made and (2) development of some methodology so that quantifiable information can be acquired which will enable others to reproduce results. An approach is suggested here based on a definition of behavior disorder theoretically described and experimentally tested in another study.[13] The definition holds that disorder results from deprivation of essential needs —both those of an organic nature and those that are socially acquired through learning and social interaction. If deprivation is of sufficient consequence, an individual will tend to perceive stimuli about himself as negative, that is, as holding threat in some way for him even though such stimuli actually do not possess negative characteristics. Consequently, if an individual in a deprived state is confronted with stimuli which can be interpreted as either negative or positive (benign), he will tend to perceive them as being predominantly negative. Hence, predominant negative perceptions reflect deprivation and the negative emotions usually associated with them. Determination of an individual's predominant perceptions of stimuli, which can be interpreted either negatively or positively, provides evidence as to whether or not the characterization of behavior disorder is appropriate.

METHODOLOGY

Technique and Procedure. The neutral stimuli used in this study are pictures of adults and children in interaction, as shown in figure 1. These stimuli provide opportunity for a subject to see the interaction between the figures as either negative or positive. Each subject is shown the pictures one at a time and asked to tell a story about each card. The negative and positive emotional expressions are then counted in each of the stories. If the number of positive expressions are represented as (a) and the number of negative expressions are represented as (b), then the formula (a−b) + 50 can be applied to an individual's emotional expressions to obtain a single score. A score of 50 means that an individual's negative and positive emotional expressions are equal. If a score of 50 or more is obtained the individual is placed in the "normal" range which was established in a normative study done earlier. If the score is less than 50, that is, 49 or less, the individual is categorized as having a behavior disorder. Thus, the lower the score, the more an individual's negative expressions exceed his positive ones.

Such an approach was used in this study with children who had ulcerative colitis. The question was asked—would their scores fall in the behavior disorder range either as a group or as individuals?

Subjects. Seven children with ulcerative colitis, 3 boys and 4 girls, were studied. They were compared with 41 normal children who were 12 years old, the mean age of the children with ulcerative colitis. The sex and age characteristics of the ulcerative colitis subjects are shown in table 1.

RESULTS

Results of this study of 7 children indicate that not only does their mean score fall in the behavior disorder range but all of the individual

TABLE 1
SEX AND AGE CHARACTERISTICS OF SUBJECTS WITH ULCERATIVE COLITIS

Sex	*N*	*Mean age*	*Age range*
Male	3	12-6	11-13
Female	4	12-6	10-14
Total Subjects	7	12-6	

TABLE 2
PSYCHOLOGICAL TEST SCORES OF ULCERATIVE COLITIS AND NORMATIVE SUBJECTS

Group	*Sex*	*N*	*Mean score*
Ulcerative colitis	M	3	47
	F	4	45
Normative	M	21	51
	F	20	51

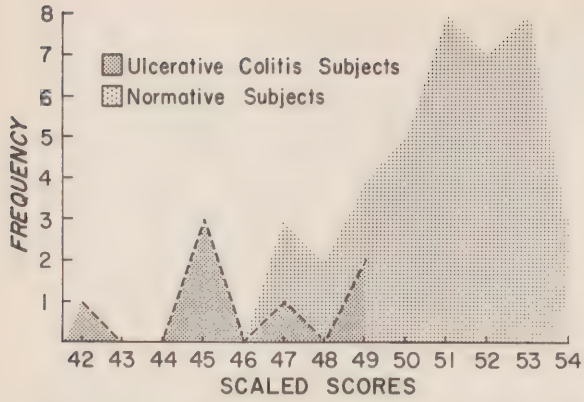


Fig. 2. Comparison of score frequencies of children with ulcerative colitis and normal children. Those with ulcerative colitis are 49 or below and therefore in the behavior disorder range. Note that the distribution of normal children is skewed to the right and above 50.

scores do as well. The mean score for the children with ulcerative colitis was 45, while the mean score for the normal group was 51. The means for the groups according to sex are shown in table 2. The comparison of the groups' scores are shown graphically in figure 2. It will be seen in figure 2 that some of the normal children fall below 50 and thus in the behavior disorder range, but most of them are above 50, with the highest frequencies being at 51 and 53. The ulcerative colitis group, on the other hand, is entirely below 50.

DISCUSSION

These findings indicate that the children in the ulcerative colitis group tend to see neutral stimuli as threatening, hostile, or depriving. Furthermore, the mean of 45 for the group shows that negative emotional expressions tend to exceed positive ones by at least 5. The normal children, on the other hand, tend to perceive the neutral stimuli as indicating favorable situations, and thus they predominantly expect cooperative or helpful experiences.

Since only a few cases are presently available, this study can only describe an approach which may be used to objectify information about psychological characteristics associated with the disease. It does suggest that children with the disease do have problems of behavior and it substantiates the clinical observations now available. Since the number of cases are so small, no conclusions can be reached about sex differences. Some sex differences, however, may exist. Arthur[14] studied 19 children, 10 boys and 9 girls, with an average age of 13 years, and found a sex difference. Her data from the Thematic Apperception Test showed differences between boys and girls in the perception of family figures. In the study described here, 42, made by a girl, was the lowest score of any of the subjects. In table 2 it will be seen that the means for both boys and girls in the normal group are the same, whereas the mean for the girls in the ulcerative colitis group was lower than the mean for boys.

The findings in this study, by making use of a way of defining and quantifying data about behavioral pathology, are in accord with those clinical observations that lead to the conclusion that psychological factors are of significance in a chronic disease such as ulcerative colitis. By defining and measuring what is seen to exist in the disease, perhaps eventually the etiology of the disease can be understood.

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The Epidemiology of Leukemia

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In the past decade numerous studies have added much to our knowledge of the possible causes of leukemia in man. It has been shown conclusively that ionizing radiation is capable of inducing leukemia, and virtually all of our knowledge concerning genetic and chromosomal aspects of the disease process has been accumulated. Considerable evidence has been secured linking viruses to certain animal leukemias, and circumstantial evidence of their association with human disease is constantly mounting. For all this, the etiology of the majority of cases remains unknown.

There are several general considerations worthy of mention. The rate of increase in incidence of 4 to 5% per year for leukemia is exceeded only by coronary thrombosis and cancer of the lung.[1–3] Leukemia is primarily a disease of the extremes of life, accounting for roughly half of all cancer deaths in children, while for those over 75 the incidence has trebled in the past twenty-five years.[4,5] Of special interest is the peak incidence of leukemia at 3 to 4 years of age in white children in the United States and England since 1940, which is lacking in the nonwhite and Japanese children.[6–9] In addition, death rates are actually declining in infants under 1 year of age.[9–11] This decline is over and above what could be expected from only early diagnosis and treatment.

Approximately one-third more males are affected by leukemia than are females, with the greatest difference in late adolescence, presumably due to acute granulocytic leukemia in adolescent males.[6,12–14] The sexes are equally affected during the first year of life, but males predominate thereafter. However, Bjelke[8] could find no sex-related difference in incidence in Norwegian children before 10 years of age.

It has been recognized for several years that an apparent excess proportion of leukemic patients come from families in the upper socioeconomic strata.[1,3] A study among children in Buffalo showed a significant excess mortality in the upper economic half.[15] In Colorado, children in the upper economic half were found to have an incidence of leukemia twice that of children below the median income.[16] In both these studies the children from the lower economic segment were found to be several years younger than their counterparts in the higher income segment. In contrast to these studies, adults in Buffalo showed no significant difference in incidence between economic halves.[12]

Geographic studies have been few to date. Some studies have demonstrated a significantly higher leukemia incidence in urban populations than in their corresponding rural areas.[12,16,17] Others have shown no differences.[8,13,15] In the United States there seems to be a gradient from a low incidence in the southeastern states to a high incidence in the northcentral and northwestern states.[9] In England and Wales, the highest incidence occurs in the south with a decreasing gradient to the north.[1]

While incidence figures are fairly constant throughout the Western World, there are several interesting facets concerning racial variations in incidence of leukemia. The rarity of chronic lymphocytic leukemia among Orientals is well documented.[18–20] African children have a very low incidence of leukemia, whereas lymphomas (Burkitt's tumor) are extremely common though they rarely display leukemic transformation in peripheral blood, even terminally.[21] In the United States, leukemia occurs twice as frequently in whites as in nonwhites, while the greatest rate of increase in recent years has been in the latter group.[9] Among whites in New York City, there is approximately 50% higher mortality from leukemia among foreign born people than among native born. This is especially true for Russian-born whites.[22] The incidence of leukemia was almost twice as high in Jews as compared with non-Jews.[22]

Table 1 shows mortality from leukemia by each country since 1930.[5,9,23–25]

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TABLE 1

LEUKEMIA MORTALITY BY COUNTRY

Crude rate/100,000/Year

	1930	1940	1950	1957
Australia	2.1	3.1	4.5	5.2
Canada	1.8	3.2	5.1	6.0
Denmark	3.0	4.6	5.9	8.4
Germany	—	—	5.2	8.9
Israel	—	—	3.9	5.7
Japan	—	—	1.5	2.4
United Kingdom	1.8	2.6	3.9	5.9
United States	2.4	4.1	5.8	6.8

GENETICS

The genetic control of leukemia probably represents the cumulative effect of several genes.[26] Studies of familial leukemia have failed to demonstrate a clear-cut, inheritable pattern.[27,28] Anderson[29] presented a family with 8 children, 5 of whom died over a period of fourteen years of acute leukemia between the ages of 4 and 8. A sixth sibling died at age 4 of recurrent pneumonia, showing toxic changes in the bone marrow but no evidence of leukemia. Miller[30] found that both mongolism and leukemia occurred more frequently in siblings of leukemic patients than in the general population. Individuals afflicted with leukemia were also noted to have a higher incidence of mongolism and other major congenital anomalies than were nonleukemic individuals.

Congenital leukemia is preponderantly granulocytic.[31] Bernhard and associates[31] found a high association between congenital leukemia and congenital anomalies and concluded that leukemia was one aspect of a genetic or chromosomal aberration occurring in utero. Videbaek (reported in Witts[2]) estimated the likelihood of a second case of leukemia appearing in a family was 16 times as great as the likelihood of the disease occurring in a family for the first time.

Stewart[32] has advanced a new hypothesis, suggesting that inheritance of a certain gene produced premalignant changes in the ancestral cells of the reticuloendothelial system. These "prezygotic" leukemias, with impaired leukokinesis, used to die in early childhood of pyogenic infections, but with antibiotics they now survive long enough to develop leukemia and die within the first five years of life. Kolmeier and Bayrd[33] reported a mother and son who developed leukemia following exposure to an insecticide spray. They postulated a genetic "preleukemic unfitness" situation existed in the pair analagous to Stewart's theory.

Twin studies have shown a significantly high concordance rate of malignancies, including leukemia among monozygous twins.[34] Pearson[35] pointed out that the occurrence of leukemia in monozygous twins has been reported more than 10 times since 1938, while if left to chance it would take more than two hundred years to produce one such set. One of the most difficult problems in assessing concordance rates is in applying the criteria for monozygosity, especially in retrospective studies. MacMahon and Levy[34] reported 5 like-sex sets of twins, all with leukemia. Monozygosity was proved in 2 sets, and there was good evidence for it in the other 3 sets. If all 5 sets were indeed monozygous, the concordance rate would approach 25% for monozygous twins.

The association of chromosomal abnormalities and human leukemia came with the discovery of the trisomy 21 condition in mongolism and the realization of the markedly increased incidence of leukemia in mongols.[36] The increased risk has been estimated to be as much as 30 to 50 times that for the general population.[37] A recent review by Miller[38] details the studies of this association.

Chromosomal abnormalities have been found associated with leukemia in nonmongols also. In chronic granulocytic leukemia an abnormal chromosome, again number 21, with deletion or translocation of one of the arms, is almost constantly found.[39] It has been designated the Ph^1, or Philadelphia chromosome. In addition, a family was recently described with an abnormally small number 21 chromosome (Ch^1).[39] Two of the 4 siblings with Ch^1 had chronic lymphocytic leukemia. The association of the 21 chromosome with 3 different types of leukemia suggests it plays an active role in leukopoiesis.

Acute leukemias are also associated with chromosomal abnormalities in nonmongols. Both the number and structural characteristics of the changes seem to be unique to each case, but constant within each individual.[39–41] In adults the changes seem to be independent of the state of the disease, while in children the chromosomes remain normal during remissions, but revert to their original pattern with relapse.

VIRUSES

Several recent reviews summarize studies linking viruses to malignancies in laboratory animals.[42,43] Viruses have been shown capable of inducing malignant transformations in human tissue culture cells and much recent epidemiologic work has been aimed at establishing the viruses as oncogenic to man.[38] Negroni[44] isolated viruses from bone marrow cultures in 10 pa-

tients with leukemia. Almeida and associates[45] presented convincing evidence of the discovery of virus-like particles persistent in the blood of 2 patients with acute granulocytic leukemia. Whether these are causal or "passenger" viruses cannot be proved.

Of special interest have been the recent reports of leukemia "clusters." Rewell[46] reported 5 patients in Wales, who had been close childhood companions; all died within a period of four years of acute leukemia, near the age of 40. A cluster of 8 children and 4 adults dying of leukemia in three years in Niles, Illinois, has attracted considerable attention. There was a particular clustering in children attending a single parochial school. In addition, a rheumatic type of disease was prevalent among the school children at the same time. There was also a significant mortality from congenital heart disease in infants of families in the school's parish.[47] Schwartz and associates[48] performed extensive serologic studies in the Niles area. The patients themselves did not demonstrate antibody titers to leukemic antigens, but as many as 3 members of each victim's family did have a demonstrable antibody. Sera obtained from technicians in Schwartz's laboratory, which were uniformly without antibody titers at the beginning of employment, became positive within six months. Unaffected families in the Niles area had no demonstrable antibodies in sera.

Seasonal peak incidences have been noted with increasing frequency over the past few years.[49] The peaks seemed to be constant when analyzed for onset of symptoms, or time of diagnosis, or death. Steinberg was unable to find any seasonal distribution in his study.[28]

Cramblett and associates[50] and Fraumeni[51] reviewed the literature concerning leukemia in infants born to leukemic mothers and were unable to find evidence of maternal-fetal transmission. Cramblett did describe the onset of acute lymphocytic leukemia in a previously healthy 9-month-old infant whose mother died of the same type of leukemia shortly after the baby was born. Rigby and associates[52] recently demonstrated the passage of quinacrine labeled leukemic cells from mother to fetus. The infant was clinically well at the time of the report.

RADIATION

Ionizing radiation has been considered leukemogenic for three decades. Lewis[53] recently confirmed the early reports of a significant excess of leukemia deaths among physicians and radiation workers, especially radiologists.[54]

The early findings were substantiated following World War II by the findings of the Atomic Bomb Casualty Commission. Among survivors of the Hiroshima and Nagasaki atomic bomb explosions there was a significant relationship between incidence of leukemia and amount of exposure to ionizing radiation.[20,55,56] The increased incidence became evident between one and one-half to three years after exposure, reached a peak incidence after five to seven years, and was still demonstrable after fourteen years. As with the cases reported earlier, the majority of individuals had either acute lymphocytic or myelogenous varieties of leukemia. Of interest was the equal sex distribution among the exposed compared with nonexposed. The Japanese population as a whole showed a typical male predominance.

Brill's group[56] calculated dose-incidence relationship curves based on distance of the subjects from the hypocenter of the blast and showed that above 50-100 rad there was a linear relationship. The risk has been calculated to be 1 or 2 cases per million, per year, per rad.

Meyer studied a population of islanders accidentally exposed to fallout from an atomic blast in Bikini, in 1954, and found no evidence of an increased incidence of leukemia ten years later.[57]

Still further proof of the leukemogenic action of radiation has come from studies of patients exposed to therapeutic and diagnostic radiation. Children receiving radiation therapy for enlarged thymus have been shown to have more thyroid tumors than the general population, but the incidence of leukemia is not disproportionally high.[58]

Court-Brown and Doll[59] found a significantly increased incidence of leukemia in patients receiving radiation for ankylosing spondylitis. On the basis of bone marrow dosages as they could be calculated, there appeared to be a linear dose-mortality relationship with the peak incidence occurring three to five years after therapy. Thomson[60] recently discussed the use of I^{131} for treatment of thyrotoxicosis. The evidence implicating this source of radioactivity was much less convincing than Court-Brown's study noted above, but isotopes such as I^{131} certainly cannot be discounted as potential leukemogenic sources.

Implication of diagnostic radiation as a leukemogenic agent is much less certain. It has often been suggested as a source to explain an unusually high leukemia incidence, but estimating bone marrow dosages in most instances has been impossible because of the retrospective aspect of the surveys. Stewart and associates[61] estimated that 8% of leukemias (excluding lymphocytic leukemia) could be traced to diagnostic radia-

tion exposure, while Gunz and Atkinson[62] believed that not more than 1% of the granulocytic leukemias could be accounted for by diagnostic procedures. Both agreed that therapeutic radiation was a significant stimulus to leukemogenesis.

Stewart and co-workers[63] found that mothers of children with leukemia had received twice as much exposure from diagnostic roentgenography as did mothers whose offspring were normal. MacMahon[64] found a 40% increase in incidence of malignancies, including leukemia, among infants whose mothers had diagnostic roentgenography during pregnancy but not in those whose mothers did not have such studies during pregnancy. He found the maximum incidence between 5 and 7 years of age. Others have pointed out that the young may be considerably more sensitive to radiation than adults,[65] and Buck[66] has estimated that the fetal tissues may have a susceptibility to radiation damage 8 times that of adult tissues. In following 500 children up to 14 years of age radiated in utero in the Nagasaki blast, Tomonaga found no leukemias.[65]

Studies in Scotland[67] and the United States[68] failed to demonstrate any correlation between background radiation and leukemia incidence. It has been suggested that areas of intense background radiation such as Kerala, India, and parts of Brazil, where doses up to 1,600 mr per year are found, be studied for possible significance.[69] A study of leukemia in India failed to demonstrate evidence incriminating background radiation as a source.[70]

Several estimates of dose-response relationships exist for cumulative radiation effect. Lewis[71] calculated the probability to be 0.7 to 6×10^{-6} per rad, per year. Court-Brown and Doll[59] estimated 1 case per million, per year, per rad. The Atomic Bomb Casualty Commission feels that for small multiple doses the threshhold for radiation induction is probably in the range of 500 rad.[72]

How much human leukemia is radiation responsible for? Some feel that radiotherapy causes 5 to 15%.[2,69] Diagnostic and background radiation estimates vary considerably with 1 estimate as high as 10 to 20% for each.[71] In children, prenatal roentgenography is believed responsible for 10% of the total cases, while postnatal diagnostic radiation and background radiation probably play very minor roles.[69]

Mole[73] has postulated that radiation damage operates by one of two mechanisms. There can be a direct effect on the cell altering its genetic make-up or reducing its resistance to infection, or by increasing any instability in the cell-multiplication process radiation only enhances the probability of an occurrence that could have happened without radiation.

SUMMARY

A summary of the general epidemiological studies on human leukemia is presented. Radiation has been shown capable of producing leukemia in humans with both total-body, single exposures and with small multiple exposures. At least for total-body exposure the dose-induction potential is a linear function.

Improved cytogenetic techniques have established the association of chromosomes and hereditary factors and leukemia to be more than chance. While the role of the virus in animal leukemia is firmly established, the evidence implicating its role in human leukemia is, so far, circumstantial. If such an association is present, continued epidemiologic investigation should establish it.

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Thrice Recurrent High Intestinal Obstruction in the Newborn

Case Presentation and Discussion

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INTRODUCTION

PERSISTENT VOMITING in the newborn is a serious problem in differential diagnosis and management. The physician must think in terms of medical causes such as chalasia, central nervous system trauma or abnormalities, septicemia, and adrenal insufficiency. Surgical causes such as stenosis or atresia of the esophagus, stomach, pylorus, duodenum, and proximal jejunum, as well as annular pancreas or malrotation of the midgut, also must be considered. Physical examination should be directed toward abdominal distension, bowel loop pattern, visible peristaltic waves, and palpable masses. The pattern, force, and color of the vomitus should be observed. Passage of a nasogastric tube into the stomach will confirm patency of the esophagus, as well as define the color and character of the gastric fluid; it is useful therapeutically to reduce distension and occasionally diagnostically to introduce radiopaque material into the stomach. Plain and upright radiographs of the abdomen are most helpful even in the early stages of high intestinal obstruction and might suggest the need for additional radiographic studies, such as a barium enema or upper gastrointestinal series. These measures proceed from the more simple to the more complex in an orderly manner and in the majority of cases will provide a satisfactory working diagnosis.

When the obstruction is compounded by multiple causes which produce recurrence of obstructive symptoms on 3 different occasions, it commands especial respect and attention.

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CASE HISTORY

A male was born May 12, 1964, weighing 8 lb. 15 oz., the seventh sibling in the family. The pregnancy, labor, and delivery were perfectly normal. He was discharged on the fifth day of life, taking a standard formula well but "regurgitating easily." On the seventh day of life forceful, nonbile-stained vomiting of ingested formula began. It worsened during the next three days, prompting admission to the local hospital. Physical examination was unremarkable except for mild dehydration. Upper gastrointestinal X-rays using a water-soluble radiopaque medium (Gastrografin) revealed "complete pyloric obstruction," with no contrast material leaving the stomach twenty minutes after ingestion (Fig. 1). Pyloromyotomy was performed for typical hypertrophic pyloric stenosis. The surgeon described the pyloric muscle as being gritty and thickened.[1] The pyloric mucosa was seen to bulge through the split pyloric muscle over the 2-cm. long incision, the completeness of the pyloromyotomy being attested by a small rent made in the duodenal mucosa. The infant was fed parenterally for two days. Oral feedings then were reinstituted. However, on the sixteenth day of life, bile-stained vomiting began, producing a weight loss of 10 oz. over a two-day period and prompting the infant's referral to the State University of Iowa Hospitals at age 18 days.

At admission he was alert and vigorous, although undernourished and dehydrated. There was mild epigastric distension and tympany with visible left-to-right gastric hyperperistaltic waves. There was a healed recent right upper quadrant paramedian incision. No masses were palpable. Bowel sounds were hypoactive. There was no gross distension of the remainder of the abdomen. Rectal examination was normal.

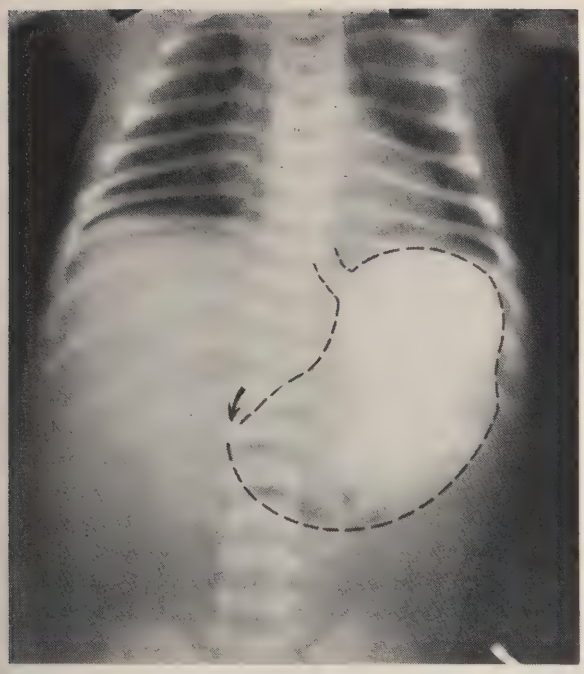


Fig. 1. Upper gastrointestinal series showing complete gastric outlet obstruction twenty minutes after ingestion. Note the distended stomach and the relative paucity of intestinal gas. The arrow marks the approximate location of the pylorus. No "string sign" is seen.

Chemical studies revealed a mild alkalosis and hypochloremia, corrected by appropriate amounts of half-strength saline containing potassium. Upright films of the abdomen (Fig. 2) revealed the "double bubble" sign characteristic of duodenal obstruction. Barium enema examination (Fig. 3) revealed malrotation with the colon lying entirely in the left side of the abdomen.

An exploratory laparotomy was undertaken through a separate transverse supraumbilical incision. Malrotation of the midgut was confirmed, with a band from the left upper quadrant cecum overlying and extrinsically obstructing the duodenum in its third portion. In addition, there was a 90° clockwise volvulus of the midgut producing lacteal and venous distension, cyanosis, and a sterile chylous ascites. After derotation of the volvulus, the bowel color improved immediately and it was possible to document a very narrow superior mesenteric vascular pedicle predisposing to the volvulus. The bands obstructing the duodenum were cut, thereby allowing the duodenum and jejunum to descend down the right parietes in an unobstructed manner. Prophylactic appendectomy was performed because of the ectopic location of the cecum high in the left upper quadrant of the abdomen. The pylorus was obscured by omental adhesions; no gross abnormality could be detected except for mild thickening. The postoperative course was marked by occasional vomiting of small amounts of ingested formula. Bowel function seemed normal, and the infant was beginning to gain weight at the time of discharge on the thirty-first day of life.

The baby did well for the first few days at home but then he began to vomit an average of once daily; the emesis was projectile and never bile stained. He seemed hungry and refed willingly after each vomiting episode. The persistent vomiting, as well as failure to gain weight, prompted the second SUI Hospital admission on the seventy-first day of life.

At readmission he was alert and well hydrated, although there was a paucity of subcutaneous fat and the buccal fat pads were prominent. Again there was definite epigastric distension and tympany with visible gastric peristaltic waves. The 2 surgical wounds were soundly healed although induration subjacent to the wounds precluded satisfactory deep palpation; no masses could be palpated. Upper gastrointestinal tract X-rays with barium (Fig. 4) revealed gastric outlet obstruction which was complete for twenty-five minutes, after which the barium trickled slowly

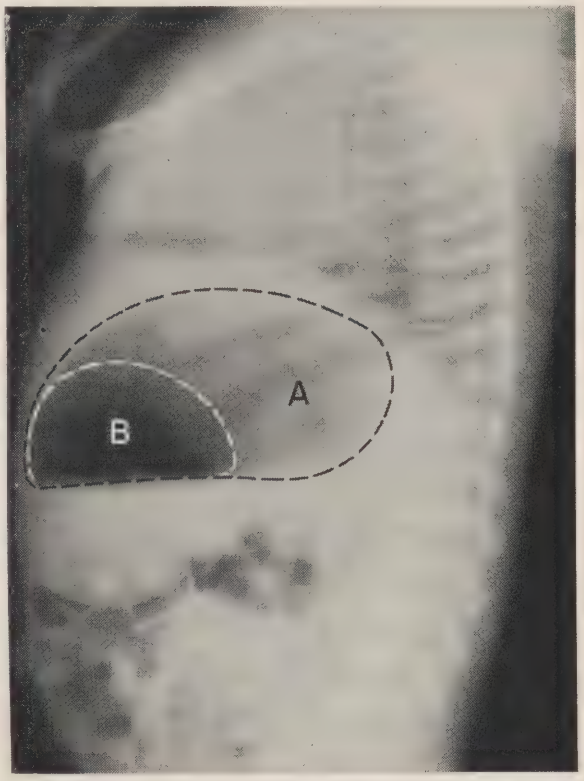


Fig. 2. Lateral upright radiograph revealing the "double bubble" characteristic of duodenal obstruction. The larger air and fluid filled cavity labeled A is dilated stomach, the smaller one labeled B is duodenum. In the A-P view the stomach bubble obscured the smaller duodenal bubble.

into a nondilated small bowel. A true "string sign" specific for pyloric stenosis was not found, although clinically our working diagnosis included a recurrent pyloric stenosis versus postsurgical narrowing of the pyloric channel. Reexploration was undertaken through the right paramedian scar. Typical hypertrophic pyloric stenosis was found, the pyloric muscle being thick, gray, and firm in consistency. Pyloromyotomy was undertaken without incident or complication. Omental adhesions on the entire anterior surface of the pylorus prevented precise localization of the previous pyloromyotomy incision. The patient tolerated this third operative procedure well, and his course in the intervening two months has been uncomplicated. During this interval he has had no vomiting and has gained over 2 lb.

DISCUSSION

This patient illustrates many points. First, he demonstrates the ability of a newborn infant to withstand multiple operations, provided certain criteria are met. Diagnosis must be made expediently before deterioration in the general condition of the patient has occurred. Nasogastric suction and repair of fluid and electrolyte deficiencies must be carried out carefully. The principles of atraumatic handling of tissues and replacement of blood loss in the operating room must be followed.

Secondly, this patient illustrates the principle that congenital anomalies are often multiple. It has been estimated that slightly more than 7% of the live-born babies in the United States are malformed in some way, and of these, fully one-fourth will have more than one malformation. Gross[2] found 28 patients (7.8%) out of a series of 156 with malrotation had some other anomaly, and Snyder and Chaffin[3] report 7 (17.5%) out of a series of 40 patients. The most common anomaly associated with malrotation is stenosis or atresia of the duodenum. This association couples intrinsic duodenal obstruction with extrinsic obstruction by the so-called Ladd's band which crosses the duodenum from the right parietes to the left upper quadrant cecum in most patients with malrotation. One patient in Snyder and Chaffin's study and 5 patients in Gross's study had hypertrophic pyloric stenosis in addition to malrotation.

By the same token, the incidence of additional anomalies with hypertrophic pyloric stenosis is reported to be 2.7%,[4] 3.4%,[5] 8%,[6] and up to 12% in the series of 1,422 babies with hypertrophic pyloric stenosis reviewed by Pollock and associates.[7] Most of these anomalies were minor and did not involve an adjacent area of the intestine. These sobering statistics should alert us to look



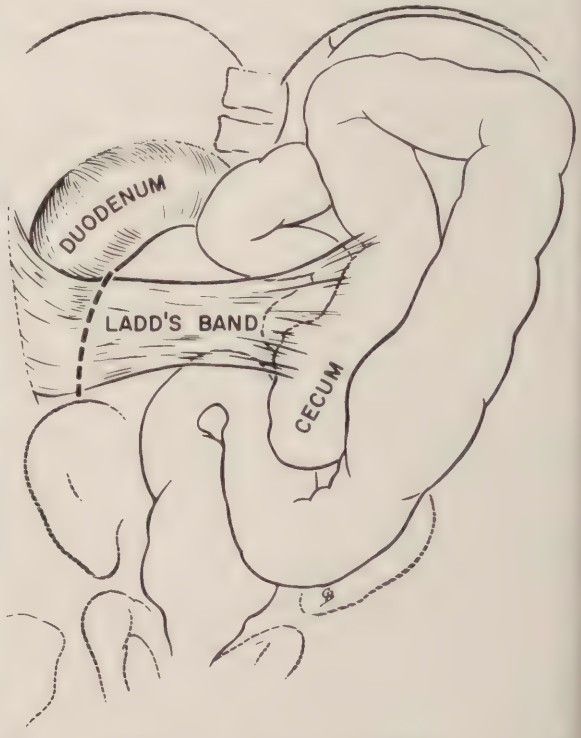


Fig. 3. (Left) Barium enema revealing malrotation. The color lies entirely in the left hemi-abdomen and small intestine in the right. The gas in the right upper quadrant is in the extrinsically obstructed duodenum. The diagnosis of volvulus cannot be made on film. (Right) Diagram emphasizing the operative findings correlated with the barium enema radiograph. The so-called Ladd's band stretches from the right posterior parieties to the left upper quadrant cecum, crossing and extrinsically obstructing the duodenum in its course. The band should be divided along the dotted line to relieve the obstruction.

thoroughly for other anomalies in every newborn with intestinal obstruction. Particularly we must consider anomalies of the same body system which in themselves duplicate the symptoms of obstruction. This is not to say that every baby with hypertrophic pyloric stenosis requires complete upper and lower gastrointestinal tract radiographic examination preoperatively, nor does the infant require complete evisceration and inspection of all the hollow viscera at the time of the pyloromyotomy. It does mean, however, that additional preoperative studies might well be indicated should the age of the patient or facets of the history or physical examination be atypical in any way. It would also justify careful inspection of the duodenal loop at the time of pyloromyotomy to be certain that it lies in a normal position and that gastric air passing through the recently opened pyloric channel also passes through the duodenum.

Thirdly, this patient illustrates the complexities of the anatomic abnormalities, grouped loosely together under the title of malrotation of the midgut, and the scope of the necessary corrective surgical manipulations. An exhaustive review of embryologic intestinal rotation is not germane to this paper. These details are well described in the textbooks of Gross,[2] Benson and associates,[8] and the splendid review by Snyder and Chaffin.[3] In the usual patient with malrotation the surgeon is presented at exploration with a bewildering array of intestinal loops lacking the anatomic landmarks of the cecum and right colon. This should immediately alert him to the possibility of malrotation which can be evaluated only by complete evisceration of the small bowel upon protective rubber lap pads before systemically proceeding with identification and correction of the abnormalities.

If the small bowel is edematous, plethoric, or cyanotic in appearance, a volvulus can be suspected. This is corrected by derotation generally in a counterclockwise direction through as many turns as is necessary; this might vary from 90° to 4 complete cycles. Volvulus accompanies malrotation in approximately 50% of the cases, causing not only a closed loop obstruction of the gut but also carrying the potential for vascular obstruction and strangulation. When the volvulus has been derotated the cecum can then be identified in the epigastrium or left upper quadrant; the band leading from the cecum across the duodenum to the right posterior parietes may then be identified (Fig. 3) and divided. Additional small adhesions often are present which angulate and kink the jejunum. These also must be released. Prophylactic appendectomy is commonly justified if the patient's condition warrants the additional ten minutes of operating time and if the cecum is not edematous or inflamed.

Volvulus occurs because of a narrow attachment of the superior mesenteric vessels due to failure of rotation of the jejunum behind and to the left of these vessels; this gives a narrow axis to the vessels around which rotation can easily occur. Recurrent volvulus is seen after surgical correction in less than 1% of cases, probably because of fixation generated by postoperative adhesions.

These maneuvers will correct the extrinsic obstruction of the duodenum and the propensity to volvulize; the small bowel will lie in the right hemiabdomen and the large bowel in the left hemiabdomen. If narrowing of the duodenum persists after the extrinsic band has been cut, the duodenum must be further investigated to rule out intrinsic obstruction.

Fourthly, this patient strongly suggests that hypertrophic pyloric stenosis can fully recur subsequent to complete correction via pyloromyotomy. The standard references discuss recurrent symptoms following pyloromyotomy in terms only of an incomplete division of muscle fibers and not as a true recurrence of hypertrophy and

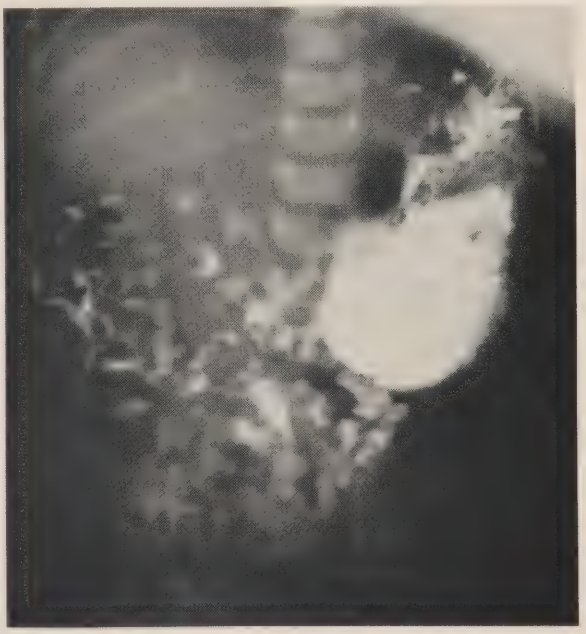


Fig. 4. Radiograph taken two hours after ingestion of barium revealing partial gastric outlet obstruction. The stomach is dilated with retained barium; no "string sign" is seen. Note the duodenum is not dilated, and the unobstructed small bowel loops largely occupy the right hemiabdomen as they should after surgical correction of malrotation.

stenosis. Thus, Pollock and associates[7] report 5 "incomplete myotomies" in their series of 1,422 babies with hypertrophic pyloric stenosis; Rinvik,[9] 2 out of 137; Savage,[10] 1 out of 61; Miller,[5] 1 out of 87; and Pollock quotes Gross as reporting 4 reoperations being necessary among 1,787 cases. None of these sources suggests a true recurrence but instead indicts an incomplete operation.

In the patient reported above, the operative report of the surgeon[1] performing the first pyloromyotomy substantiates the diagnosis of hypertrophic pyloric stenosis. In addition, he describes the criterion used to indicate completeness of the muscle splitting, such as bulging of the pyloric mucosa through the muscle defect. A rent was also made in the duodenal mucosa, a point used by some surgeons in the past to indicate complete division of the pyloric muscle fibers. Pasma[11] states that some Dutch surgeons deliberately open the dudodenal mucosa for this very reason. Although technical factors made evaluation of the pylorus difficult at the time of the malrotation correction, it was the authors' opinion that no residual hypertrophy of the pylorus existed at this time. The sixty-three-day interval between the 2 pyloromyotomy operations suggests 2 episodes of pyloric obstruction. Changes in color of the vomitus from nonbile-stained before the first pyloromyotomy operation to bile-stained before the malrotation operation and back again to a colorless emesis before the second pyloromyotomy all support the contention that the 2 pyloric stenoses were indeed separate and distinct rather than a continuum.

SUMMARY

Vomiting in the newborn is a sign which must be carefully evaluated in relation to its cause, management, and correction. The case history reviewed illustrates the complexities which are occasionally encountered in the management of infants with high intestinal obstruction. The patient had 3 distinct episodes of high intestinal obstruction due to 2 episodes of hypertrophic pyloric stenosis separated by sixty-three days in time and by an intercurrent episode of duodenal obstruction due to malrotation and volvulus. This patient emphasizes the need to search for other malformations when 1 anomaly is discovered, in remote body systems as well as closely associated systems. Evidence is presented which supports the probability of recurrent hypertrophic pyloric stenosis rather than simply an incomplete initial pyloromyotomy. Meticulous medical and surgical care can be rewarded by a thriving infant in the face of recurrent and multiple causes for high intestinal obstruction.

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Management of Diabetes in Children

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A THERAPEUTIC PROGRAM for the child with diabetes mellitus is adequate only if it insures normal physical and emotional growth and development and thus results in a well-adjusted healthy adult. This objective can be attained if due consideration is given not only to insulin and diet but also to the psychological needs of the child. Except in the unusual circumstance, the diabetic child does not present major behavioral problems. However, the physician who assumes the care of one of these children must be aware of the special psychological needs they have and be able to supply the emotional support which they require.

In planning the therapy of the diabetic child, the principles to be followed and the objectives to be reached must be clearly defined. The program should be simple and rational so that the child and his parents can understand it and carry it on at home. It should result in the blood sugar being reasonably stable throughout the entire day, with no wide swings from very low to very high levels. The total amount of insulin given should be that amount which will allow sufficient utilization of ingested glucose to insure normal growth, prevent hepatomegaly, avoid acetonuria, and allow freedom from the symptoms of polyuria and polydipsia. While no exact statement can be made with respect to how much glycosuria is excessive, amounts of glucose in a twenty-four-hour urine specimen which are much in excess of 10% of the daily carbohydrate intake are generally incompatible with these criteria. Equally important, however, is the avoidance of frequent hypoglycemic episodes, for these may not only result in significant brain damage but also cause such a high level of anxiety in the child and in his environment that his normal emotional growth and development may be jeopardized. Minimal glycosuria and freedom from shocks are not incompatible.

Diet therapy. Dietary therapy is based on the current concept of the action of insulin. It is believed that insulin has only one site of action, namely, the cell membrane. Insulin apparently alters the permeability of the membrane, thus allowing glucose to enter the cell. Once it is inside the cell, glucose is converted to glucose-6-phosphate and is then metabolized without any further requirement for insulin. Two pathways are open to it: the Embden-Meyerhof and the hexose-monophosphate (HMP) shunt. In recent years the importance of the HMP shunt has been increasingly recognized, for in consequence to glucose passing through this pathway, TPN.H is formed and is used later in the conversion of butyryl CO.A to crotonyl CO.A in the synthesis of fatty acids. Thus, the well-known inability of the diabetic organism to synthesize fat is seen to be the result of impaired glucose metabolism rather than a specific effect of insulin on fat synthesis. While insulin aids the entrance of certain amino acids into cells, this is apparently not a major action. There is no direct effect of insulin on either protein or fat catabolism.

The practical implication of these data is that, if insulin is needed only in carbohydrate metabolism, only the carbohydrate intake of the diet need be closely regulated in the treatment of diabetes. When this is done a relatively constant daily dose of insulin can be maintained despite considerable variations in total caloric intake. It further follows that the dietary exchange can be based entirely on the carbohydrate content of foods; this results in a tremendous simplification in making exchanges. It also allows a wider range in the daily total caloric intake, depending on the child's appetite, activity, and mood.

Initial evaluation of the new patient with diabetes includes a careful investigation of the previous dietary habits, food preferences, and family customs of nutrition. Children old enough to express their own desires are asked how much bread, cereal, and other high carbohydrate food they wish to eat with each meal. The choice of carbohydrate foods in the hospital, and subsequently at home, should take into account the preferences of the child and his family with a single important provision that, once determined,

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the intake must be constant or nearly so from day to day.

Each meal is so arranged that it contains 5 carbohydrate-containing food groups, namely, (1) milk, (2) bread, (3) cereals, potatoes, or equivalents, (4) fruit, and (5) vegetables (except at breakfast). Additionally, each meal contains meat, eggs (not more than 5 per week), or fish, the quantity of which may vary according to the patient's appetite. The fat intake may vary also, but both patients and their families are encouraged to limit this component of the diet to not more than 35% of the total calories consumed, to substitute whenever possible polyunsaturated fats for saturated fats, and to restrict their intake of foods containing large amounts of cholesterol. The nutritional adequacy of the diet so achieved is examined and, if found lacking, is corrected by educating the family to a more desirable one.

The milk group includes buttermilk, fresh milk, and powdered milk. To use one in place of the other (in "exchange"), the following would be appropriate amounts.

Milk, whole, fresh	1 cup
Buttermilk	1 cup
Powdered milk, whole	¼ cup, dry
Powdered skim milk	3 tablespoons, dry
Fresh skim milk	1 cup
"Fortified" skim milk	⅔ cup

This group represents 12 gm. of carbohydrate per serving in breads, cereal, potatoes, or equivalent.

Bread	1 slice
Potatoes	½ cup, mashed or 1 small
Yam	¼ cup
Corn	⅓ cup or ½ medium ear

This group represents 15 gm. of carbohydrate per serving.

Fruits. This group of foods is listed as measured servings and can be interchanged with one another. These fruits are used in the fresh, dried, cooked, frozen, or canned forms, as long as no sugar or syrup has been added.

Pears	1 small
Apple, 2-in. diameter	1 small
Banana	½ small
Grapes	12 medium
Mango	½ small
Peach	1 medium
Plums	2 medium
Melon, 6-in. diameter	¼ melon
Watermelon	1 cup, diced or 1 slice, 3 × 1½ in.
Orange	1 small

This group represents 10 gm. of carbohydrate per serving.

Vegetables. This class of foodstuffs is divided into 2 groups. The first group or group A consists of vegetables which for ½-cup servings yield 3 to 6 gm. of carbohydrate. The second group or group B consists of vegetables which for ½-cup serving yields 7 to 9 gm. of carbohydrate.

Group A	
Cabbage	Tomatoes
Lettuce	Cauliflower
Mint	Cucumber
Spinach	Eggplant
Radishes	
Group B	
Squash	Peas
Beet roots	Turnips
Carrots	Onion
Pumpkin	

Seven grams or less of carbohydrate is not replaced if left by the patient. Second helpings of ½ cup for the A group of vegetables and ¼ cup for the B group of vegetables are given. This allows the patient to "fill up" on relatively low carbohydrate foods.

The simplicity of the basic dietary rules and their lack of "specialness" encourage the normal adjustment of the child with diabetes to this disease and foster normal family interrelationships. Siblings are not deprived of food or money to permit a special diet for the child with diabetes. The child soon learns to make his own carbohydrate "exchanges" and may substitute an evening snack at a neighbor's house for one of the suppertime helpings independently and safely. With increasing growth or improvement in appetite the total carbohydrate content as well as the total calories of the diet are increased gradually. Under these circumstances it would be expected that there would be an appropriate increase in the insulin requirement. Transient hunger, however, is satisfied by protein snacks and second helpings of the low carbohydrate vegetables. It is advisable to instruct parents that when the child grows and consistently demands more food he should be given more. There is no reason for the child with diabetes to be hungry.

With this diet the use of so-called "diabetic" foods and soft drinks is unnecessary because the normally available products can be included in the exchanges. For instance, the adolescent child, having gone to a restaurant with his peers, may exchange a cola drink for a glass of milk if he so desires. The frequent consumption of such foods is not encouraged, however, because they are not considered to be nutritionally desirable. Children expecting to participate in strenuous sports are advised to eat an extra helping of meat or other protein food beforehand and to drink sweetened tea or fruit juice throughout the course of the game; it is far better for them to

have glycosuria than for them to be unable to participate in the games due to fear of hypoglycemia. The onset of upper respiratory infection may be associated with temporary anorexia, but, because the carbohydrate portions are usually the most acceptable items of the diet, a constant carbohydrate intake is usually not difficult to achieve. Older children with diabetes who tend to be obese may need dietary restrictions even as their nondiabetic colleagues would. Dietary regulation and general diabetic management are more difficult in small children because of the greater lability of the metabolism. Therefore, in their treatment, it seems preferable to permit moderate glycosuria rather than to risk hypoglycemic episodes.

It is thus seen that the policy of this clinic is not to control diabetes by manipulations of the diet. On the contrary, the child is encouraged to eat the amount of foods which satisfies his appetite. Sufficient insulin is then given to meet the patient's requirement under these dietary circumstances.

Insulin therapy. Insulin therapy of diabetic children requires careful and thoughtful consideration if it is to be successful. "Rules of thumb," such as 5 units for each 1+ of sugar in the urine, may be satisfactory for the treatment of adults with diabetes but are not adequate in childhood diabetes. In this age group the types of insulin used, their dosage, and the time of administration must be altered to meet the needs of the individual child. No one program of insulin therapy is satisfactory for all diabetic children.

One of the first steps in undertaking the regulation of the newly diabetic child is to decide how much insulin should be given and what types of insulin should be employed. It has been reported that the average insulin dosage of diabetic children is 0.4 units per pound of body weight. This amount of insulin is used as an initial dose level and has proved to be satisfactory. This dosage may be inadequate in the first two or three weeks, and consequently larger amounts of insulin may have to be administered. Later the patient usually goes through a period in which there is a marked decrease in his insulin requirements and, under these circumstances, his dosage must be reduced. After a variable length of time his insulin requirements again rise and often exceed previous levels. When increasing and decreasing insulin dosage, it is desirable to keep in mind that the effect of insulin varies as a logarithm of its dose. Thus, when the dose is small, changes should be made by not more than 1 unit per day. However, if the dose is large, significant increases in effect will be obtained only when the increments are in the magnitude of 2 to 5 units.

A relatively large number of insulin preparations are presently available. These include crystalline zinc, globin, neutral protamine Hagedorn (NPH), semilente, ultralente, lente, and protamine zinc insulins.

Because of its increased stability, crystalline zinc insulin (CZI) has now largely, if not entirely, replaced "regular" (amorphous) insulin. Injected subcutaneously, it achieves its maximum effect in three hours and, except when given in excessive amounts, its effect is largely dissipated by eight or nine hours. When it is administered intravenously, its maximum effect is seen in one hour. It should be noted that it is the only insulin preparation that can be given intravenously. Its particular areas of usefulness are in the treatment of diabetic coma and in combination with other insulins in the long-term treatment of diabetes.

Globin and NPH are commonly called "intermediate" insulins and are similar in their effects on blood sugar levels. In the first hour or two after administration they cause no appreciable change in the blood sugar. An increasing effect is then noted which reaches its maximum at about eight hours. The hypoglycemic effect then diminishes and is not apparent by eighteen hours in most patients. Both of these insulins may be mixed with crystalline zinc insulin; when this is done the total and temporal effect of crystalline zinc insulin is not appreciably altered. Thus, it is possible to prepare an insulin mixture which has the quick acting effect of CZI and the longer acting effect of globin or NPH. However, it must be stated that the author has abandoned the use of globin insulin because of his repeated experience that relatively severe hypoglycemic shocks may occur unexpectedly and with essentially no preliminary symptoms to warn the patient.

The lente insulins are a relatively new and interesting family of insulins. Hallas-Møler has reported insulin in acetate buffer at a pH above 4.4 and in the presence of 2 parts of zinc per million precipitates. Within the pH of 4.7 to 5.7 the otherwise amorphous precipitate is crystalline and essentially stable. Both the amorphous and crystalline preparations remain completely insoluble in the pH range from 5 to 8. In clinical trials it has been found that the amorphous form has a more rapid effect (semilente) than does the crystalline preparation (ultralente). Unpublished studies carried out in this clinic have shown that in children the maximal hypogly-

cemic effect of semilente usually occurs four to five hours after injection, while that of ultralente usually occurs at sixteen to seventeen hours. Since the semi- and ultralente are mutually miscible, mixtures of the two in varying proportions have considerable differences in time of maximum activity. One such mixture is lente insulin. This preparation is 30% semi- and 70% ultralente. Its range of activity seems to be almost identical with that of NPH insulin. If CZI (pH 2.7 to 3.5) is mixed with the lente insulins the added soluble insulin is converted to either amorphous or crystalline zinc insulin, depending on the final pH of the mixture, and this cannot be reliably predicted. Therefore, it is not possible to prepare an insulin mixture which has both the quick acting effect of CZI and the more prolonged effect of either ultralente or lente insulin.

Protamine zinc insulin (PZI) is a long acting insulin, with maximum effect being observed in the second twelve hours after its administration, with lowest blood sugar values being usually observed at twenty to twenty-three hours. It is usually unsatisfactory when used alone in childhood diabetes but can be effectively employed in combination with crystalline zinc insulin. There being an excess of protamine in the commercial preparation when PZI and CZI are mixed in a syringe, part of the latter insulin is converted to PZI. In the past it has been common to mix 2 parts of CZI with 1 part of PZI on the assumption that approximately one-half of the CZI would combine with the excess protamine. However, the ratio of the excess protamine varies from 1.5:1 to 1.9:1. Thus, mixing of commercial CZI and PZI yields final proportions of short and long acting insulins which are extremely variable and the administration of such a mixture produces unpredictable effects on the blood sugar. This difficulty can be avoided by administering the two insulins in separate syringes and sites.

From this brief review of the characteristics of the presently available preparations of insulin, it may be seen that to obtain the objectives of insulin therapy which have been described above a combination of CZI with one of the intermediate insulins or PZI, or both, is necessary. One such combination of insulins which is usually satisfactory is CZI and PZI when administered in separate syringes and at separate sites. For initiation of treatment 40% of the total insulin is given as CZI, the remainder as PZI. All urine voided in the intervals from breakfast to lunch, lunch to supper, supper to one hour before breakfast, and one hour before breakfast to breakfast is collected in separate containers, and each is tested for sugar and acetone. Subsequent adjustments of the two insulins are made in accord with the results of the urine tests. If the patient is spilling in the specimen voided immediately before breakfast, the PZI is increased; the dose of CZI is adjusted in accord with the daytime urines. A midmorning snack is nearly always necessary to permit use of a large enough dose of CZI so that it will be still exerting an appreciable effect during the afternoon and yet not cause a late morning hypoglycemic episode. After regulation as judged by the urine tests seems to have been achieved, the blood sugar is measured at 10 A.M., 2 P.M., 4 P.M., 7 P.M., 11 P.M., and 7 A.M. Unrecognized hypoglycemia and the extent of the diurnal variation of the blood sugar is thereby determined, and a decision can be made as to the adequacy and appropriateness of therapy.

When at home, the patient on this insulin program tests his urine for reducing substances four times a day. The specimens tested are the prenoon, the presupper, the bedtime, and the second voided specimen before breakfast. He takes that amount of protamine zinc insulin which is one more unit than results in a trace of sugar in the second voided prebreakfast specimen. If that specimen is aglycosuric on four successive mornings, he reduces his protamine zinc doses by 1 unit every second day until he again shows a trace and then increases it by 1 unit. When this is done, insulin shock due to PZI is very rare. The CZI dose is adjusted according to the noon test, again being 1 more unit than results in a trace.

The patient using CZI and PZI in this way usually shows glycosuria at bedtime. If this is associated with enuresis, nocturia, or a twenty-four-hour glycosuria which is greater than 10% of the carbohydrate ingested, the program must be considered unsatisfactory and appropriate changes made.

Generally a more satisfactory insulin regimen is a mixture of CZI and NPH before breakfast and NPH alone before supper. From experience it has been found that about 65% of the total daily dose of insulin should be given before breakfast. The usual proportions of the mix are 15 units of CZI to 50 units of NPH. Subsequent alterations are made according to the lunch and supper urine tests. For example, if the patient consistently spills at noon but is aglycosuric at supper, the CZI in the mixture is increased 5 units and the NPH decreased by 5 units to yield a 20:45 mix. No change is made in the total amount of insulin administered until the tests at these two periods are the same. Similarly, if the patient shows a tendency to be hypoglycemic in the early morning hours, replacing the supper

NPH by the same mixture used in the morning or by CZI alone may be effective. An occasional patient is very satisfactorily controlled using only a morning injection of the CZI:NPH mixture.

Insulin therapy consisting of NPH, globin, or lente insulin as a single injection before breakfast has been found unsatisfactory. The blood sugars of patients receiving any of these 3 insulins in this way are characterized by high levels in the midmorning, normal or hypoglycemic levels in the late afternoon, and gradually rising levels during the evening to a maximum hyperglycemia before breakfast. Efforts to decrease the total twenty-four-hour glycosuria result in frequent hypoglycemic episodes in the midafternoon.

Mention must be made of the alterations necessary in insulin dosage when the patient is suffering from an intercurrent illness. If the diabetic child develops a febrile illness such as a pharyngitis, the amount of insulin which was previously adequate may no longer be. This is reflected by an increased glycosuria and frequently acetonuria. Should the urine show 3 or 4+ sugar and the presence of acetone, the child should receive not only his usual insulin dosage but also an additional amount of CZI. The recommended amounts of extra CZI are 10, 15, or 20% of his total daily insulin requirement, depending on whether the acetonuria is trace, moderate, or strong. Thus, if the child who is taking a total of 40 units of insulin per day has both a glycosuria and a moderate acetonuria at his noon test he should receive 6 units of CZI before this meal. Additional amounts should be given before supper and at the parents' bedtime if the same conditions obtain. At the same time the patient should receive appropriate treatment for his infection.

Another common problem requiring alterations in the insulin therapy is that of the child who has a gastrointestinal upset and is, in consequence, vomiting. If this begins in the early morning, and so often it seems to, it quickly becomes evident that the child probably will not be able to eat and retain his usual breakfast. Such a patient should be given nothing by mouth until he has not vomited for two hours. Then, at precisely fifteen-minute intervals, he should be given 1 or 2 teaspoonfuls of a sweet carbonated beverage for the next two hours. After this, larger amounts may be given and his normal diet gradually restored. This simple program minimizes the length of time that the vomiting will continue. At the same time his insulin must be continued. If the patient is showing glycosuria he should receive his usual insulin dosage at the regular time. On the other hand, if he is aglycosuric the amount of insulin administered should be reduced by 50%. Subsequently, it may be necessary to administer small doses of regular insulin, as described above, if glycosuria and especially if acetonuria occur. Should the vomiting persist and the patient become aglycosuric and particularly if he also develops acetonuria, a retention enema consisting of 2 ounces of corn syrup and 1 ounce of water will prevent serious hypoglycemia. Management of intercurrent illnesses in these ways will almost entirely prevent the occurrence of diabetic acidosis.

If the insulin therapy is to be satisfactory at home as well as in the hospital, it is of the utmost importance that the parents and the child, if he is of responsible age, understand it. They should be taught exactly when each of the insulins used has its maximum effect as well as the duration of the effect. They should know how to increase and decrease the insulin according to the varying needs of the child. They should be especially aware of the need for altering the amount given under the circumstances of intercurrent infections. Evaluation of their knowledge and their use of it should be made at each return visit, and advantage of every opportunity should be taken to clear up any possible misunderstandings.

Treatment of diabetic acidosis. Treatment of coma is guided by its cause, which is an inadequate supply of insulin to meet the needs of a particular situation, such as an infection. Under these circumstances, fatty acid synthesis is impaired, resulting in an accumulation of acetylacetyl CO.A and its metabolites, acetone bodies. Additional amounts of acetone bodies result from the catabolism of fat. The net result is the development of an organic acid acidosis. Treatment, therefore, is directed toward the reestablishment of normal fatty acid synthesis and decreased fat catabolism by means of insulin and glucose and the replacement of the fluid and electrolyte losses as well as supplying adequate maintenance amounts of these substances during the treatment period. After twelve hours of intensive therapy the patient should be taking fluids orally, be free of ketonuria, and be reasonably bright and alert.

Crystalline zinc insulin in the dosage of 100 units per square meter of body surface must be given immediately, half intravenously and half subcutaneously. The total amount of insulin which is subsequently given must be based on continuing observation of the patient's status and cannot be predicted by any known rules. Usually the initial dosage is repeated in two hours, with smaller doses given thereafter.

The second important component of the treatment of diabetic acidosis is the replacement of the large water losses and the relatively smaller losses of electrolytes by administering intravenous fluids. The following procedure is recommended: Begin with a solution containing 100 mEq. per liter sodium, 60 mEq. per liter chloride, 40 mEq. per liter lactate, and 3.5% glucose and administer at the rate of 400 ml. per square meter of body surface per hour. This should be continued for two hours or until the patient is voiding freely. After that the intravenous solution is replaced by another consisting of 5% glucose, with 57 mEq. of sodium, 25 mEq. of potassium, and 40 mEq. of chloride per liter, as well as phosphate. This is administered at the rate of 2,500 ml. per square meter per twenty-four hours. An indwelling catheter is inserted, and the urine is checked every hour to insure that the patient at all times has glycosuria. The rate of progress is measured by improvement in respiration, pulse, and blood pressure. While pH and serum electrolyte determinations are helpful, they are not absolutely necessary, for adequate treatment may be carried out, if necessary, by means of clinical assessment and repeated testing of the urine for glucose and acetone. It is important that these patients not be given isotonic saline, for such a solution does not supply adequate amounts of water.

Psychological therapy. Although diabetes mellitus by itself does not cause emotional problems in children, it does tend to reinforce and expose any instability which may be present in the family environment. There are a number of influences which may cause conflict and distress in children with diabetes and lead to increased emotional tension. If a diet is used which does not allow sufficient calories to satisfy his appetite, he may feel deprived, psychologically as well as physically, and this may lead him to steal food or other objects. Even with a liberalized diet, such as is used in this clinic, there must be a restriction of certain foods which he may desire. The routine and regularity of the regimen may produce conflict, especially among adolescent diabetics who are rebelling against conformity in any instance. The recurrent necessity to test the urine and to take insulin serves as a constant reminder that there is "something wrong" with them. This implied criticism is even more marked if the presence of glucosuria is considered "bad." To go to the trouble of testing the urine only to find that glucose is present is not, under these circumstances, likely to increase the desire to perform this task. For this reason, the words "good" and "bad" should not be used to signify the presence or absence of glucose in the urine. Of more significance is whether appropriate changes in the insulin regimen were made in consequence to the urine test results. Emphasis is thus placed on the fact that the urine tests are done so that data are available to enable the diabetic to know what to do, rather than as a measure of "goodness" or "badness." No opportunity is missed to compliment them when the changes have been appropriate. If the tests have been done but not used to judge the amount of insulin needed, the purpose of the testing is pointed out, and the patient is encouraged to make use of the information.

It is sometimes difficult for children to understand why, when they feel so well, it is necessary for them to receive an injection each day. This is countered by thoroughly explaining to the parents and also to the child, if old enough, the true nature of diabetes and why it is that insulin must be taken by injection. It is often useful to suggest that diabetes is a "condition" rather than a disease in order to emphasize that they are not ill and that they can do anything other children can.

Separation from the parents during hospitalization may arouse anxiety and fear. This may be more evident in the parents than in the child. Consequently, it is desirable to have liberal visiting hours and for all personnel concerned with the care of the child to take advantage of this in order to establish a friendly rapport. The hospitalized child is often confused by the roles of the host of new and strangely garbed people and feels threatened by the therapeutic injections, laboratory tests, and unfamiliar environment.

Almost invariably the parents feel guilty that their child has developed diabetes. It is important to recognize this and to say to them that it was not anything which they did or did not do which led to the onset. It is desirable to explain the role of heredity and to explain that since it is inherited as a recessive characteristic both of the parents must be carriers. This is particularly important when there is a strong family history in one parent's family and none apparent in the other's.

It is important to recognize these various areas of emotional conflict and to provide both patient and parents with sympathetic support if one is to be successful in the general management of the child with diabetes. If such tensions and anxieties are permitted to flourish, they may ultimately be expressed directly in quarrels within the family group or through internal effects producing serious metabolic imbalances. It is im-

possible to obtain good control of diabetes in the emotionally disturbed child. Many workers have shown that the discussion of subjects of emotional significance can produce dramatic alterations in the level of sugar in the blood of patients with diabetes. Problems in home management involving cheating or other antisocial behavior on the part of the child or failure to follow directions on the part of parents may stem directly from such emotional conflicts. As diabetes must always be a lifetime problem, it becomes important to the patient, family, and community that all the persons concerned accept the fact that the disease will be a persistent problem demanding constant awareness and treatment. The doctor and nurse should be sympathetic and encourage the parents to discuss their feelings about the occurrence of diabetes in their child. Such an approach is essential in setting the stage for proper instruction of the parents in the care of their child, as learning will not take place effectively during periods of emotional stress. The main reason for hospitalization of the diabetic child is to allow the establishment of this rapport between the doctor, the patient, and the parents in consequence to which effective teaching becomes possible.

In the long-term care of the child with diabetes the preservation of an effective relationship between the doctor, nurse, patient, and parents is essential. The doctor and nurse must give evidence of a sincere personal interest in the family's problems, maintain a friendly noncritical attitude, and encourage the development of emotional maturity and enlightened self-confidence. Common problems in dealing with diabetics and their families can be solved successfully only by recognizing that emotional tensions affect the disease and by incorporating appropriate simple mental hygiene in the regimen of diabetic management.

THREE PITFALLS MUST BE AVOIDED for successful surgical management of varicose veins: inaccurate diagnosis, incomplete removal, and inadequate follow-up. Diagnostic errors may include (1) failure to make proper examination and tests to identify the affected saphenous system and to detect incompetent perforating veins, (2) underestimation of stasis complications, and (3) failure to recognize deep venous insufficiency. Incomplete removal is the main reason for recurrence, and careful marking of all involved veins with an indelible dye solution is essential. Improper ligation in the groin can be avoided by making the incision high enough and long enough for good exposure and by widely dissecting all tributaries before ligating the main channel. All tributaries coursing down the thigh from the groin must be removed, as well as the entire incompetent saphenous system and enlarged or varicose veins on foot and ankle, and all incompetent perforating veins must be resected. Adequate follow-up should include injection therapy and elastic support when necessary and long-term prophylactic care with periodic reexaminations throughout life. With care taken to avoid pitfalls, results were good in 94% and fair in 5% of 1,080 operations for incompetent great saphenous veins in a follow-up period averaging twenty-five months.

KARL A. LOFGREN, M.D., Mayo Clinic and Foundation, Rochester, Minn. J. Amer. med. Ass. 188: 17-21, 1964.

Polyuria

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Polyuria is often difficult to identify, especially in the infant who subsists on a predominantly fluid diet and excretes relatively large volumes of dilute urine. The parent of the toddler may note increased fluid intake or an unusual number of wet diapers, while the complaint in the older child is likely to be frequency or nocturnal enuresis.

Table 1 presents a classification of major causes of polyuria in children based upon the primary functional defect in each disorder. Diabetes insipidus, excessive water ingestion, and diabetes mellitus with glycosuria are ordinarily characterized by massive polyuria, while the other diseases are associated with lesser degrees of polyuria. In fact, disorders which interfere with normal function of the renal medulla (Group 3 in table) are often unrecognized until irreversible changes have occurred. On the other hand, solute diuresis (Group 4) is obviously rapidly reversible with treatment of the primary disorder. Whatever the symptom, if polyuria is suspected routine urinalysis and a test of renal concentrating ability should be performed. It must be emphasized that absence of albuminuria, glycosuria, and abnormality of the urinary sediment are not sufficient to exclude renal abnormality as a cause of polyuria.

Because much variability exists among normal infants and children in relation to frequency of urination, enuresis, and thirst, the significance of these manifestations is often in doubt. Even if accurate information about the exact volume of urine excreted in twenty-four hours could be obtained, interpretation of this information would frequently be difficult or even impossible. Of more value from the practical point of view is determination of the ability or inability of the child to produce a normally concentrated urine when subjected to a standardized test of renal concentrating ability.

CONCENTRATION OF URINE OF NORMAL INDIVIDUALS

Osmotic pressure of extracellular fluid in the normal individual is maintained between 272 and 294 milliosmols per liter[1] because the kidney, under the influence of circulating antidiuretic hormone (ADH), is able to adjust the rate of water excretion to compensate for variations in intake. As serum osmolarity decreases, secretion of ADH decreases also and, as a result, urinary concentration falls, with maximum dilution being approximately 50 milliosmols per liter (specific gravity about 1.002). As serum osmolarity increases, secretion of ADH increases and urine becomes more concentrated, with maximum concentration being approximately 1,400 milliosmols per liter (specific gravity about 1.040). Concentration of urine through the influence of circulating ADH is possible because of the osmolar gradient maintained in the renal medulla by the countercurrent mechanism.[2]

Most full-term infants over 1 month of age are able to achieve urinary concentration of 1,000 milliosmols per liter.[3,4] Although concentrating ability of younger fullterm and some premature infants may be limited to 650 milliosmols per liter, most can achieve concentrations of at least 800 milliosmols per liter.[5–7]

TEST OF URINARY CONCENTRATING ABILITY

Determination of the concentrating capacity of the kidney is essential in evaluating polyuria. Prolonged water deprivation may produce severe dehydration if the concentrating mechanism is abnormal; therefore, the period of thirsting must be regulated to some extent by the patient's tolerance of the procedure. In our clinic the usual urinary concentration test performed with children is as follows: A "dry" supper, including nothing that can be poured and no jello, custard, or similar food, is given no later than 6:00 P.M. on the day before urine is to be tested. Then, no food or fluids are permitted until completion of the test. At 6:00 or 7:00 A.M. the child voids and the urine is discarded. The next voided specimen of urine is utilized for determination of effective osmolarity. If effective osmolarity is less than 1,000 milliosmols per liter (specific

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TABLE 1
CAUSES OF POLYURIA IN CHILDREN

1. Diabetes insipidus
   A. Vasopressin-sensitive diabetes insipidus
   B. Vasopressin-resistant diabetes insipidus
2. Psychogenic water ingestion
3. Renal medullary disease
   A. Hypokalemic nephropathy
      1. Renal tubular acidosis
      2. Fanconi syndrome
      3. Hyperaldosteronism
      4. Chronic diarrheal diseases
   B. Hypercalcemic nephropathy
      1. Idiopathic hypercalcemia
      2. Vitamin D intoxication
   C. Anatomic and vascular disturbances
      1. Pyelonephritis
      2. Chronic hydronephrosis
      3. Sickle cell disease or trait
4. Solute diuresis
   A. Glycosuria
   B. Chronic renal failure

gravity approximately 1.030), vasopressin is administered subcutaneously and 1 or 2 additional specimens of urine are collected. Values less than 1,000 milliosmols per liter are considered evidence of decreased urinary concentrating ability.

The test is modified for infants. A period of thirsting of eight to twelve hours is employed and vasopressin is administered at 3 hourly intervals during this time. Concentration of urine less than 800 milliosmols per liter (specific gravity 1.024) is considered evidence of decreased urinary concentrating ability.

The dosage of vasopressin employed in these tests is as follows: One unit every three hours for infants under 1 year of age, and 5 units every three hours for the average 10-year-old child, with intermediate doses for children between the ages of 1 and 10 years. Overdosage is most commonly evidenced by the occurrence of hypertension or abdominal pain.

RELATION BETWEEN URINARY CONCENTRATING ABILITY AND POLYURIA

When individuals consume normal diets some components of the diet are not utilized for growth or repair of tissues and will be excreted in the urine. The solutes thus excreted are spoken of as the "renal solute load" provided by the feeding. These solutes are primarily minerals, especially sodium, chloride and potassium, and end-products of protein metabolism, especially urea.

When usual diets are consumed it has been estimated[8] that a 6 kg. infant ingesting 800 calories may be required to excrete 260 milliosmols per day. If maximal urine concentration were 150 milliosmols per liter (specific gravity 1.004), approximately 1,730 ml. would be required for urinary excretion of the solute load. If maximal concentrating ability were equal to that of plasma (280 milliosmols per liter; specific gravity 1.010), minimum urinary volume would be 930 ml., whereas urinary concentration of 600 milliosmols per liter would require the renal expenditure of only 430 ml. per day.

DIABETES INSIPIDUS

When an adequate amount of circulating ADH is present and the distal convoluted tubule and collecting tubule are normally responsive to ADH, the permeability of these segments of the nephron to water increases and the urine becomes concentrated.

Vasopressin-sensitive diabetes insipidus. In vasopressin-sensitive diabetes insipidus, the amounts of circulating ADH produced by the body are inadequate and urine therefore is persistently dilute. Administration of vasopressin corrects the deficiency, allowing tubular fluid to equilibrate with its hypertonic environment.

Vasopressin-resistant diabetes insipidus. Vasopressin-resistant diabetes insipidus is a familial disease in which the kidneys are morphologically and functionally normal except for inability to respond normally to vasopressin. The disease appears to be inherited as an X-linked dominant with full expression in the male and partial expression in the female; however, not all cases conform to this pattern.[9] Some patients with vasopressin-resistant diabetes insipidus demonstrate partial response to hydropenia;[10] consequently a test of renal concentrating capacity must be interpreted in the light of other findings. Other patients do not demonstrate response to parenteral administration of vasopressin but are able to concentrate urine above 280 milliosmols per liter when dehydrated (probably a result of decreased volume of glomerular filtrate).[11]

The following brief case report is included to emphasize the fact that polyuria may go unrecognized for prolonged periods in the infant. In this case the presenting complaint was fever.

Case report. A 6-week-old male infant was admitted to the State University of Iowa Hospitals because of fever of undetermined origin. Prenatal course and birth were normal. Birth weight had been 3.9 kg. There was no history of convulsions, diarrhea, or vomiting. Intake of milk formula had been approximately 24 oz. daily and

the parents had not considered the volume of urine or frequency of urination unusual.

Rectal temperature was 103° F., weight 4.9 kg., and skin was doughy with poor turgor. Initial urinalysis did not reveal any abnormality but insufficient quantity was available for determination of specific gravity. Concentration of urea nitrogen in serum was 35 mg. per 100 ml. and concentrations of sodium and chloride were 161 and 122 mEq. per liter, respectively. Carbon dioxide content and serum concentrations of potassium, calcium, and phosphorus were normal. Excretory urograms were interpreted as normal. Since osmolarity of urine did not exceed 132 milliosmols per liter during a forty-eight hour period when aqueous vasopressin was administered at three-hourly intervals, the diagnosis of vasopressin-resistant diabetes insipidus was accepted. In this case, the exceptionally low osmolarity of the urine aided greatly in arriving at a diagnosis. If urine osmolarity had approached the osmolarity of plasma during administration of vasopressin, establishing a diagnosis would have been more difficult.

PSYCHOGENIC WATER INGESTION

Excessive water consumption is present in several disorders in which concentrating ability is decreased and may be considered a consequence of the polyuria rather than its cause.

Excessive ingestion of water in psychogenic water ingestion may produce temporary renal insensitivity to vasopressin and be associated with inadequate circulating vasopressin in response to increasing serum osmolarity. Psychogenic water ingestion is characterized by normal serum osmolarity (in diabetes insipidus the serum osmolarity is usually slightly elevated); concentration of urine to an osmolarity greater than that of plasma during water deprivation; and decrease in urinary flow and increase in urinary concentration as a response to infusion of hypertonic saline.

HYPOKALEMIA

Decreased urinary concentrating ability is the most constant and significant functional renal impairment in hypokalemia, probably resulting from malfunction of the countercurrent mechanism and functional abberations in the collecting tubules.[12,13] In humans the consistent pathologic lesion is swelling and hydropic degeneration in the epithelial cells of the proximal convoluted tubule.[14] The degree and duration of potassium depletion determine the extent of impairment in concentrating ability. The dysfunction is nearly always reversible but concentrating ability may remain abnormal for months or years after correction of potassium deficiency.[15] Knowledge that concentrating ability may remain abnormal for some time should not lead one to overlook the existence of chronic pyelonephritis or other abnormality.

Commonly recognized causes of hypokalemic nephropathy are renal tubular acidosis and Fanconi syndrome (inclusive of cystinosis). Other causes are chronic diarrheal disease, congenital hypokalemia of renal origin,[16] hyperaldosteronism, and prolonged administration of drugs that promote excretion of potassium.

The following case report may represent congenital hypokalemia of renal origin, or vasopressin-resistant diabetes insipidus with superimposed hypokalemia. The case is presented to illustrate the difficulty often encountered in establishing a diagnosis even when many diagnostic procedures are carried out. In this case the absence of juxtaglomerular hyperplasia in the tissue obtained at renal biopsy was considered sufficient to exclude the diagnosis of hyperaldosteronism without hypertension.[17]

Case report. An 8-year-old boy was admitted to the State University of Iowa Hospitals at 5 years of age because of nocturnal enuresis and growth failure. Birth weight had been 4.2 kg. Failure to grow normally and large intake of fluid, mainly milk, were noted during the first year of life, but no significant illnesses occurred. An older sister with similar complaints had died at 6 years of age. Administration of vasopressin in oil for several months before admission had had no effect on the polydipsia or polyuria.

Physical examination revealed no abnormality except that the child was small. The height was 102 cm. and weight was 15 kg. Blood pressure was normal. Urinalyses did not disclose any abnormality except low specific gravity and persistent alkalinity. The volume of urine ranged from 2 to 5 liters daily. Urinary cultures failed to demonstrate significant bacteriuria. Maximum urine osmolarity did not exceed 284 millosmols per liter with administration of vasopressin. Serum concentration of potassium was low (3.1 to 3.2 mEq. per liter on 4 occasions), while carbon dioxide content was slightly elevated (25-29 mM. per liter). Concentrations of calcium and phosphorus were normal. Roentgenograms were interpreted as normal at 5 years of age but demonstrated moderate nephrocalcinosis at 8 years of age. Clearances of inulin and para-aminohippurate were 103 (normal 100-130) and 481 (normal 550-750) ml. per 1.73 meter square per minute, respectively. Urinary excretion of aldosterone was elevated. Microscopic

evaluation of renal tissue obtained at biopsy revealed no juxtaglomerular hyperplasia, but was consistent with a diagnosis of hypokalemic nephropathy.

Administration of spironolactone A has resulted in an increase in the concentration of potassium in serum to 4.3 mEq. per liter but there has been no clinical evidence of response to this treatment. The nephrocalcinosis is thought to be a consequence of large milk intake in the presence of persistent alkalinity of the urine.

HYPERCALCEMIA

One of the earliest signs of hypercalcemia is impaired ability to concentrate urine. The defect may be permanent with nephrocalcinosis and progressive renal failure or may be promptly corrected by definitive treatment such as removal of a parathyroid adenoma. The concentrating deficit results from (1) excessive thirst, (2) decrease below normal of the osmolarity of the renal medulla, and (3) decreased permeability to water of collecting tubules.[18] The most common causes of hypercalcemia in children are idiopathic hypercalcemia and vitamin D intoxication. Other causes are excessive administration of calcium, especially in the newborn, Boeck's sarcoid, milk-alkali syndrome, and the hypercalcemia associated with skeletal immobilization.

RENAL MEDULLARY DISEASE

Any disease which distorts renal medullary anatomy or changes medullary blood flow may render the concentrating mechanism less effective. Occasionally the initial complaint of patients with chronic pyelonephritis may be polyuria.[19] Ability to concentrate urine is often impaired to a greater extent in this disorder than in other chronic renal diseases, presumably because the renal medulla is more damaged than is the cortex.

The following case illustrates that pyelonephritis may present with polyuria and that no abnormality may be found by routine urinalysis.

Case report. A 13-year-old girl was first admitted to the State University of Iowa Hospitals at 8 years of age because of polydipsia, polyuria, and nocturnal enuresis of gradual onset after attacks of measles and chicken pox four years previously.

Physical examination was normal except for her small size. The height of 112 cm. and weight of 15 kg. were equivalent to a height-age of 5½ years and weight-age of 3½ years. Specific gravity of the urine did not exceed 1.005 even when vasopressin was administered. Urinalyses and cultures of urine were normal. Concentration of urea nitrogen in serum was 21 mg. per 100 ml. Concentration of calcium and phosphorus in serum was normal. At 8 years of age clearances of inulin and para-aminohippurate were 25 (normal 100-130) and 94 (normal 550-750) ml. per 1.73 square meters per minute, respectively; similar values were found at 13 years of age. Microscopic examination of tissue obtained at renal biopsy was interpreted as showing evidence of chronic pyelonephritis.

A concentrating defect, reversible early in life but progressive and irreversible later, occurs in sickle-cell disease.[20] Other disorders such as medullary sponge kidney, medullary cystic disease, or hydronephrosis may also present with polyuria. Of these disorders "chronic hydronephrosis"[21] may simulate vasopressin-resistant diabetes insipidus; distal tubular function may improve once the obstruction has been removed. This disorder should not be confused with the massive sodium and urea diuresis which may follow relief of urinary tract obstruction.

SOLUTE DIURESIS

Glycosuria of uncontrolled diabetes mellitus may result in urinary output of 3 to 10 liters per day. In chronic renal failure, urinary volume ranges from 1 to 3 liters per day. The solute load requiring renal excretion is great, resulting in rates of flow that overwhelm the concentrating mechanism. In these disorders the greater the solute excretion per nephron the more closely the urinary composition resembles that of plasma. Disorders of solute diuresis are reversible if the underlying disease can be satisfactorily treated, as is the case in diabetes mellitus.

SUMMARY

Causes of polyuria in children have been classified in relation to the primary functional defect in each disorder. A procedure for testing renal concentrating ability has been outlined and several illustrative case reports have been presented.

It is important to distinguish between the various causes of polyuria because severe concentrating defects may be present for long periods of time before other signs of renal disease, such as proteinuria and azotemia, are noted. Early recognition and treatment of a number of these disorders may restore concentrating ability and, in most instances, help preserve residual renal function.

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TRAUMATIC ASPHYXIA may result from sustained compression of the chest or upper abdomen in an accident. The patient may be comatose for several hours and may have apnea leading to hypoxia and generalized cyanosis which rapidly diminishes as breathing is resumed. The crushing injury forces blood out of the right atrium, superior vena cava, and azygos system in a retrograde direction through veins and capillaries of the chest, neck, and face. Vascular distension and atony of the capillary walls occur, as well as stasis of blood in veins and capillaries and extravasation of erythrocytes from vessels. Petechiae and ecchymoses result. Reddish-purple to black discoloration extends over the face and neck and sometimes over the upper portion of the body. Subconjunctival hemorrhage nearly always occurs, and periorbital edema and ecchymosis are frequent. Retinal edema may cause temporary loss of vision. Exophthalmos and damage to the optic nerve from hemorrhage into the retrobulbar region is possible, as is miliary ecchymosis of the tympanic membrane and transient hearing loss. The prognosis is good if the patient survives the battering of the accident, and treatment is directed toward intrathoracic injuries. Skin discoloration and subconjunctival hemorrhages require no treatment. Of 6 patients with traumatic asphyxia, 5 recovered and 1 died from pulmonary complications.

JAMES R. SHAMBLIN, M.D., and DWIGHT C. MC GOON, M.D., Mayo Clinic and Foundation, Rochester, Minn. Arch. Surg. 87:967-975, 1963.



Olivia T. Peterson, R.N.

LAURA HEGSTAD, R.N.

Minneapolis

THE FACT that a nuclear physicist in New York City, a naval commander stationed in San Diego, a blind girl in Richmond, and a truck driver in Minneapolis are able to bathe a newborn infant with all the confidence of an experienced mother is a tribute to the work of Miss Olivia T. Peterson, who served as director of the American Red Cross home nursing program from 1941 to 1953.

Since 1953, Miss Peterson has been living in semiretirement in Starbuck, Minnesota. However, during the twelve years that the home nursing program functioned under her leadership, literally hundreds of thousands of people across the nation acquired skill in giving elementary nursing care to the sick and training in maternal and child health techniques.

As one of the nation's leading advocates of the back-to-the-bedside movement, Miss Peterson has devoted almost her entire career, as a nurse and, later, as an administrator, to helping people acquire a basic knowledge of home nursing techniques. Home nursing, she maintains, is a household art, a skill as important to the homemaker as basting a roast or a hem.

Miss Peterson's preoccupation with family health stems from years of experience in public health nursing with the Red Cross and with the Minnesota Department of Health. As a public health nurse working in rural Minnesota in the 1920s, she came to realize that there would never be enough visiting nurses to meet the everyday requirements of the ill in the home and that a large part of the nursing of simple ailments would have to be done by some member of the family.

Miss Peterson was serving as director of public health nursing for the Minnesota Department of Health when she received a call from the Red Cross in the fall of 1941. In accepting the directorship of the home nursing program headquartered in Washington, D. C., she had not intended to be away from the state department of health for more than three months. However, Red Cross officials soon realized that in her, their organization had not only a capable administrator but a nurse who had long advocated by precept and example the kind of training that was so much in demand. As a result, the "three months" stretched into years.

Although the Red Cross home nursing program has been in existence since the early part of the century, it was not until the beginning of World War II that people, remembering former influenza outbreaks, began registering in large numbers for nursing courses. Over 1 million people were given home nursing instruction during the war years alone and, in the years that have followed, enrollments have averaged over 100,000 each year.

Miss Peterson's association with the Red Cross

LAURA HEGSTAD *is with the Minnesota Department of Health, Minneapolis.*

began with America's entry into World War I in 1917. During this period, the Red Cross recruited a number of nurses for army service. Assigned to the British Expeditionary Forces, she served at a base hospital at Rouen and later at a United States leave area at Chamonix, France.

Upon returning to Minnesota after eighteen months of service in France, she became a Red Cross public health nurse in Pope County. The job of county nurse might have seemed rather tame after overseas military duty had it not been for the influenza epidemic that swept through the state in 1920. Dr. Henry M. Bracken, then executive officer of the state department of health, described the epidemic as "the most serious we have ever been up against."

The 1920 influenza epidemic, although not as serious as the two that had preceded it, nevertheless claimed over 1,000 lives. In all, over 12,000 persons died as the result of influenza between 1918 and 1920.

One community in Pope County had been completely immobilized by the epidemic. Miss Peterson had to organize those who were still on their feet to take care of those who were not. The Red Cross provided all food that was not donated by the townspeople. Meals were prepared by ladies' aides. Boy Scouts delivered food to the homes, carried water, brought in wood, and maintained the fires. A livery stable owner volunteered a team of horses and a bright red sled. The horses flew Red Cross flags at their ears, and all traffic gave the sleigh the right-of-way.

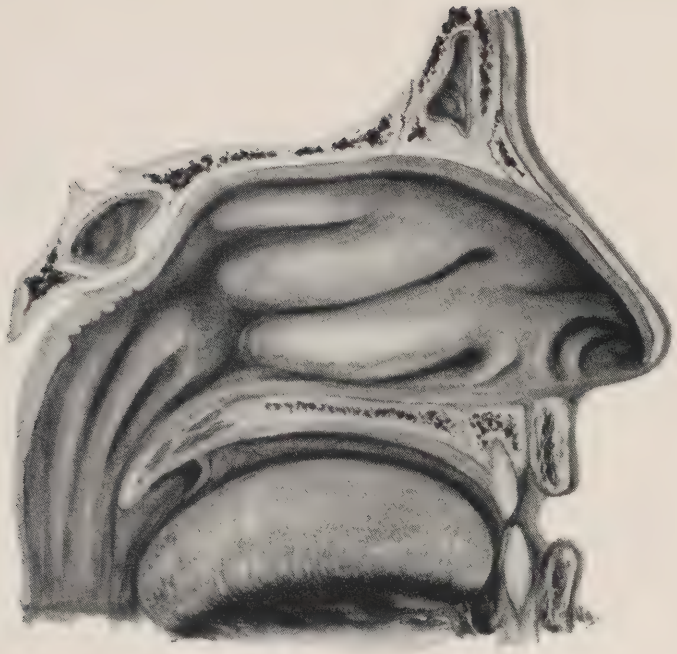
In recalling her experiences in Pope County, Miss Peterson states that she never expects to see a community throw itself with greater dedication into a common cause.

Miss Peterson's abilities as a public health nurse and as an administrator were recognized by the state board of health in 1926 when it appointed her director of the state health department's public health nursing program. Under her leadership, public health nursing programs in the state were constantly improved and expanded. She worked closely with the University of Minnesota's school of public health in establishing a program in public health nursing and, with others, helped develop state laws governing the organization and standards of public health nursing.

A native of Starbuck, Minnesota, Miss Peterson received her basic nursing education at the St. Paul Hospital in St. Paul, since closed. She received her public health nursing training at the University of Minnesota.

Miss Peterson has served as president of the Minnesota Nurses Association and the State Organization for Public Health Nursing. She was an active member in the American Public Health Association and is a life member of the National League for Nursing and an honorary member of the Quota International.

Although retired, she maintains an active interest in Red Cross service at the St. Cloud Veterans Hospital. She has also conducted Red Cross courses at the newly erected Minnewaska Nursing Home at Starbuck and for the local Red Cross chapter.



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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses of the drug. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasm, hypotensive crises (1 fatal case), anuria, stomatitis, proctitis, and anaphylaxis. Treatment should be symptomatic and the drug not reinstituted. Isolated cases of agranulocytosis and thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Massive overdosage may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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Book Reviews . . .

Pediatric Therapy

edited by HARRY C. SHIRKEY, *1,144 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1964. $16.50*

Medical treatment is not synonymous with drug therapy and, happily, this 1,100-page book does not concern itself solely with pharmacological therapeutics. Dr. Shirkey, in his twin capacities as editor and contributor, has dwelt extensively on the art or psychological side of treatment, as well as the scientific aspects. He states succinctly that "the physician, as he enters the sick room, can be either a ray of sunshine or a blundering idiot" and that this is why one doctor's therapy is better than another's even though both use the same drugs.

The book is divided into 19 sections. The first 3—drug treatment, treatment of symptoms, and general therapy—concern themselves with the treatment of the patient in general. Use of tris-buffer is discussed in detail, as are obesity, parenteral fluid therapy, and anesthesia.

The chapter on the placebo should be required reading for all students as well as practitioners of medicine—the latter so they may reexamine the complex interaction between physician and patient in the light of their own experience and the former so they may learn to utilize this valuable tool.

Symptomatic treatment is dealt with in detail. Again, kindness and the comfort of a physician's hands in conjunction with drugs are emphasized as a synergistic team that is often more effective than either method of action alone.

The chapter on the treatment of fever is well done. It is emphasized that high temperatures as such are usually not dangerous unless they approach 106 to 107° F. Even fevers of 108° F. have been reported as remaining at those levels for prolonged periods without lasting sequelae to the patient. Dr. Shirkey is no nihilist where fever is concerned, however, and he states that, when the child remains unhappy, fussy, or irritable, therapy with aspirin or perhaps sponging is indicated. I think most would agree. Other chapters on treatment of cough and pain are included. The care of chronically ill children is dealt with, and a chapter on recreational therapy is worth reading.

Following the section on infectious diseases, the chapters are arranged by body systems. The contributors are well known and highly qualified.

A section on surgery includes a few paragraphs on bedside resuscitation, which serves to remind us that oxygen is still the best stimulant for the young infant. Prepubertal unilateral breast enlargement is discussed as is neonatal hypertrophy of the breasts. The management of strabismus is dealt with and early referral is emphasized.

Various lists of drugs are categorized into those that cross the placenta, those that are secreted in breast milk, and those that discolor urine and feces when excreted. The text is completed with a 50-page table of drug dosages arranged, like the sections, in terms of the systemic action of medications (endocrines, cardiovascular, antineoplastics, and so on). Both dosage by square meter and dosage by body weight are used. A nomogram is inserted for convenient estimation of surface area.

(Continued on page 16A)



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(Continued from page 15A)

There is little to find fault with in this well-edited and well-written book, and the contributors are well known and highly qualified. It may very well become the accepted general text in the field of pediatric therapy, and I feel that all who treat children should have ready access to it.

L. H. GREENE, M.D.
Minneapolis

Manual of Clinical Nutrition

by ROBERT S. GOODHART *and* MICHAEL G. WOHL, *279 pp., ill., Lea & Febiger, Philadelphia, 1964. $5.50*

This manual on clinical nutrition is clear and concise, and the actual diets listed and analyzed for certain specific diseases make it a useful reference for physicians as well as other persons in the field of nutrition. In this compact book, the authors bring together current knowledge about diet in health and disease.

The authors of this book, both of whom are physicians, have written a more comprehensive textbook on the subject. They state, however, that in this manual, which is not intended as a textbook, "many physicians may find that the information contained herein meets the requirements for their daily practices."

The first part gives an overall estimation of nutritional status. In this section, there are chapters on (1) nutritional requirements in health, (2) normal values for some common indices of nutritional status, (3) the diagnosis of malnutrition, (4) inborn errors of metabolism, and (5) the nutritional anemias.

The second part describes the principles of therapeutic diets in a number of disorders. The tables included are quickly readable, and many are given which include the food values of the foods allowed in the various diets. This material supplies authoritative data on diets in a form for easy reference by doctors and nutritionists.

There is a final chapter on nutrition in the care of the surgical patient, with a current bibliography. The appendix includes the revised (1963) "Recommended Daily Dietary Allowances" from the food and nutrition board of the National Research Council.

In general, this book is a good clinical guide. It is brief and, therefore, should be useful for the active practitioner who is interested in up-to-date concepts of clinical nutrition. It belongs in a general medical library.

ROSE L. SLESNICK
Cincinnati

Gastric Surgery: Errors, Safeguards, and Management of Malfunction Syndromes

by MOSES E. STEINBERG, *342 pp., ill., Appleton-Century-Crofts, Division of Meredith Publishing Co., New York, 1963. $12.95*

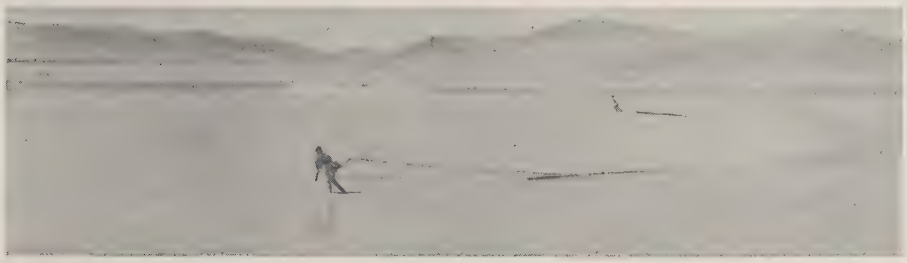
Dr. Moses E. Steinberg evaluates and summarizes the observations, mistakes, and sucesses of a career in gastric surgery that has extended more than forty years. His study concerns his personal series of about 1,300 post-gastrectomy patients and covers 84% of them. This extensive experience and the unusual effort he made to study the postoperative course make this book excellent fare for the active abdominal surgeon.

The first section of the book has a fine review of the early history of gastric surgery. It contains translations

(Continued on page 18A)



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FREE PARKING

(Continued from page 16A)

of original papers by the major pioneers in gastric surgery and serves to clarify the eponymic chaos present in most current literature that deals with gastric surgery. This is an admirable section.

The second part is a discussion of postgastrectomy malfunction syndromes. Dr. Steinberg defines these as (1) gastric pouch malfunction, (2) dumping syndrome, and (3) mechanical malfunction of the afferent and efferent anastomotic loops. His lengthy discussion of the symptomatology and differential diagnosis of these syndromes provides the reader with a keen insight into the postgastrectomy complaints of patients. All physicians and surgeons caring for such patients will find Dr. Steinberg's ideas illuminating.

The third and fourth parts concern Dr. Steinberg's surgical efforts to correct the factors that have caused postgastrectomy malfunction. He describes, in detail, a form of gastroenterostomy which he believes minimizes these malfunction syndromes. He has chosen to call this procedure a "pantaloon" anastomosis.

Dr. Steinberg does not discuss vagotomy and its attendant gastric procedures. However, the discussion relating to postgastrectomy malfunction is pertinent to problems encountered following vagotomy. As is true of much of medical writing, at times the literary style and the syntax contained in this book make for "heavy going." However, the dividends accruing make worthwhile the necessary effort to overcome these deficiencies.

RICHARD J. WEBBER, M.D.
St. Louis Park, Minnesota

Pathophysiology of Peptic Ulcer

edited by STANLEY C. SKORYNA, *497 pp., ill., J. B. Lippincott Co., Philadelphia, 1963. $20*

This is the published report of a symposium on pathophysiology of peptic ulcer, held at the Second World Congress of Gastroenterology. The individual articles on gastric physiology, experimental ulcer production and methodology, effect of pharmacological compounds, and local and systemic factors in ulcer formation are written by a distinguished international panel from 19 countries. The subject matter is presented clearly and concisely and is minutely documented and extensively illustrated. This volume fulfills the need for a contemporary résumé and evaluation of current investigative methods and results. As such, it would appear to be of great value as a reference and to those interested in experimental medicine.

NELSON H. STONE, M.D.
Chicago

Psychiatry for Students

by DAVID STAFFORD-CLARK, *277 pp., ill., Grune & Stratton, Inc., New York City, 1964. $5.75*

Textbooks in psychiatry are legion, but on occasion a new and worthwhile volume does become available. In this rather concise and condensed book, Dr. Clark summarizes in a careful manner, and from the viewpoint of a British psychiatrist, many of the concepts subsumed under the discipline of psychiatry. Since the scope and nature of the book are directed toward the student, there is little attempt made to present diverse views or to argue specific points. The author begins with a general description of the nature of psychiatry and of the clinical

(Continued on page 20A)



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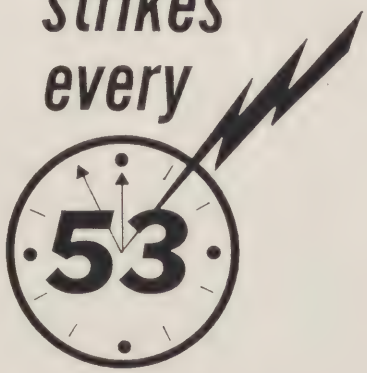


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(Continued from page 18A)

approach. His chapters on personality development and psychodynamics seem quite limited to an American, if one considers the great interest in this country in these subjects, and although his chapters on the functional psychoses and neuroses are organized in a logical manner they suffer from an overinclusive simplification of the material.

The strong points of this book are the discussion of differential diagnoses, such as the differential diagnosis of hypochrondriasis, and the discussion of therapy. As is usually not the case in psychiatric texts, therapy is amply treated; this is done from the viewpoint of the clinician. Specific dosages and techniques are both listed and amplified. Also, the author provides a very fine chapter on hypnosis, as well as a summary of the field of child psychiatry.

The biggest failings of the book are the rather unique nomenclature that does not correspond to the official nomenclature used in this country, the author's general tendency to oversimplify, and his failure to provide a properly cited, sufficient bibliography. The index, though serviceable, is not inclusive, and cross-indexing is virtually nonexistent.

In general, Dr. Clark's book is less a textbook than a primer for clinicians. It would be valuable on the bookshelves of most nonpsychiatric clinicians and especially useful on the shelves of those who have not had the opportunity to participate in psychiatry or to review psychiatric knowledge intensively. All told, this should prove to be an interesting and rewarding book for the nonpsychiatric clinicians, and it could very well be recommended to those who wish to review the current body of psychiatric knowledge or to obtain some idea of current therapies.

JAMES JANECEK, M.D.
Minneapolis

The Role of the Gamma System in Movement and Posture

by IAN A. BOYD, CARLOS EYZAGUIRRE, PETER B. C. MATTHEWS, *and* GEOFFREY RUSHWORTH, *71 pp., ill., Association for the Aid of Crippled Children, New York, 1964. $2.50*

This compact monograph brings together recent physiology related to the motor system and, in particular, movement and posture. Very lucid presentations of the morphology of muscle spindles and tendon organs, functional characteristics of muscle receptors, central regulation of skeletal muscle activity, and modification of the gamma system activity in man are presented clearly by very competent and respected physiologists.

The excellent figures and descriptive legends are generously dispersed throughout the text and add to the manner of presentation. The book is one that may be appreciated by students interested in the very complex studies of the peripheral, central, and muscular mechanisms related to spasticity and their alterations of posture and movement.

This small volume ends with a very comprehensive bibliography; the pertinent remarks and additions by the commentators make it a valuable addition for any student who is currently interested in the motor system and its alteration in disease. The reasonable price and attractiveness of the book make it a must for any library.

J. T. JABBOUR, M.D.
Oklahoma City

News Briefs . . .

North Dakota

DR. LEONARD W. LARSON, a Bismarck pathologist and past president of the American Medical Association, has been named president-elect of the American Cancer Society. Dr. Larson also is past president of the American Society of Clinical Pathologists, has been a member of the American Cancer Society board since 1959, and is a founding fellow of the American College of Pathologists. He is a 1922 graduate of the University of Minnesota Medical School and in 1956 received the university's alumni outstanding achievement award.

Minnesota

OFFICERS of the Minnesota Academy of General Practice for the coming year were named during the annual meeting held in Minneapolis in September: Dr. Ellsworth A. Thayer, Fairmont, president; Dr. Edwin W. Kilbride, Worthington, vice-president; Dr. Henry W. Quist, Jr., Minneapolis, secretary-treasurer; Dr. John W. Anderson, Blue Earth, vice-president of house of delegates; and Dr. Herb L. Huffington, Waterville, president-elect.

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DR. DONALD B. SWENSON, a Mankato pediatrician for nine years, has joined the Mankato Clinic staff. He is a native of Waseca, where his father, Dr. Orvie J. Swenson, has been in general practice for thirty-seven years. Dr. Donald Swenson is a graduate of the University of Minnesota Medical School. He interned at Milwaukee County General Hospital and took a two-year residency in pediatrics at the University of Minnesota Hospitals.

° ° ° °

DR. ROBERT W. SPLETTSTOESSER has joined Dr. Roger B. Hallgren to practice in Belle Plaine. Born in Waconia, he earned a B.S. degree in pharmacy from the University of Minnesota in 1952, served in the Army in 1953 and 1954, and received his M.D. degree from Baylor University, Houston, in 1962. He interned at Cook County Hospital, Chicago, and has been practicing in Big Fork, Minn., since early summer.

° ° ° °

DR. WENDELL K. DOWNING, a graduate of the University of Iowa Medical School, has joined Drs. Howard M. Frykman and Stanley M. Goldberg of Minneapolis in the practice of proctology. Dr. Downing received postgraduate surgical training at Hennepin County General Hospital, and training in proctology in the Ferguson Clinic, Grand Rapids, Mich.

° ° ° °

DR. VERNON D. E. SMITH of St. Paul has been named president of the Minnesota Medical Foundation—a 2,300-member organization providing private assistance to the

(Continued on page 22A)

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(Continued from page 21A)

University of Minnesota Medical School. He was among alumni and faculty members who founded the group in 1939 and has been vice-president since 1962. He succeeds Dr. Corrin H. Hodgson of Rochester.

* * * *

DR. WILLIAM E. JOHNSON has announced plans to leave Morgan after thirty-three years of practice for a staff appointment at the St. Cloud Veteran's Administration Hospital. This leaves the community without a doctor and civic efforts are under way ot secure one.

* * * *

DR. HANNS P. BARTHOLDT has opened practice in Cook, moving from Soudan. A naturalized United States citizen, he received his medical degree from the University of Munich, Germany, in 1952 and completed internship and residency in general surgery, orthopedic surgery, and internal medicine before coming to this country in 1956. He then interned in St. Louis, Mo., and took a general and orthopedic surgery residency at the Bismarck Hospital, Bismarck, N.D. Dr. Bartholdt was in Princeton, N.J., before moving to Minnesota in 1963.

* * * *

DR. ROLLAND H. WILSON, a Winona physician since 1929, announced his retirement in October. He is a past president of the Minnesota State Medical Society, head of the Winona department of health from 1950 to 1960, and served for twenty years on the medical advisory committee of the Minnesota department of public welfare. Dr. Wilson received his M.D. degree from the University of Minnesota in 1923. He practiced in Harmony for five years and took a year of postgraduate work in surgery and gynecology before opening his Winona practice.

Deaths . . .

DR. DUANE D. RUBBERT, 33, of La Moure, N.D., died in the crash of a light plane Nov. 1. The plane he was piloting two days after his first solo flight crashed in a heavy fog. Dr. Rubbert, a bachelor, received his M.D. degree from the University of Kansas in 1958. He was a member of the American Academy of General Practice.

* * * *

DR. ARTHUR T. LAIRD of Duluth, an early investigator in tuberculosis control, died Oct. 17 at age 91. Born in Madison, Ohio, he received his M.D. degree from the University of Pennsylvania in 1900. His early investigative work included studies of mosquitoes and yellow fever with Army surgeon Dr. Walter Reed and tuberculosis control under Dr. Henry Hun, an early advocate of sanatorium treatment. Dr. Laird came to Duluth in 1911 and became the first superintendent of the Nopem-



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ing Sanatorium, a position he held for more than thirty years. During World War I, he took leave to conduct tuberculosis examinations at Fort Snelling and later went to France under Rockefeller Foundation auspices working on the commission for the prevention of tuberculosis. Dr. Laird belonged to many civic and professional groups, including the St. Louis County and Minnesota Medical Societies, American Medical Association, American Thoracic Society, and American Hospital Association.

* * * *

DR. EMIL HABERMAN, 86, died in Osakis, Minn., Oct. 27. He had practiced there from 1916 to 1959. A native of Wisconsin, he attended school at Leola, S.D., and received his M.D. degree in 1904 from the University of Illinois. Dr. Haberman began general practice in Bancroft, S.D., for three years, then practiced in DeSmet, S.D., and Minneapolis before moving to Osakis. He was active in many Osakis civic affairs and in 1954 was honored by the village for fifty years in medicine.

* * * *

DR. DAVID E. ELLISON, for twenty-five years a Minneapolis assistant city health officer, died in Minneapolis, Nov. 6, at age 72. He also was medical director of the Twin City Rapid Transit Co. from 1950 to 1955, when he became president of the company. Born in Minneapolis, Dr. Ellison received his M.D. degree from the University of Illinois and practiced in Minneapolis from 1920 to 1950.

* * * *

MEMORIAL SERVICES were held in St. Clair, Minn., Nov. 16, for Dr. Richard O. Juliar, who died a few weeks previously at his Los Angeles home. He had been in general practice in the St. Clair area for more than forty years before moving to California. Dr. Juliar received degrees in medicine and pharmacy from the University of Minnesota, practiced for a few years in North Dakota, and then began his St. Clair practice, also operating a drugstore and serving as postmaster.

* * * *

DR. ARTHUR S. KISTLER, a St. Paul general practitioner for fifty-three years, died Nov. 14 at age 93. Born in Tannersville, Pa., he received his M.D. degree from the University of Pennsylvania in 1898, locating in St. Paul the following year. During practice, Dr. Kistler was a staff member at Bethesda Lutheran Hospital, St. Paul.

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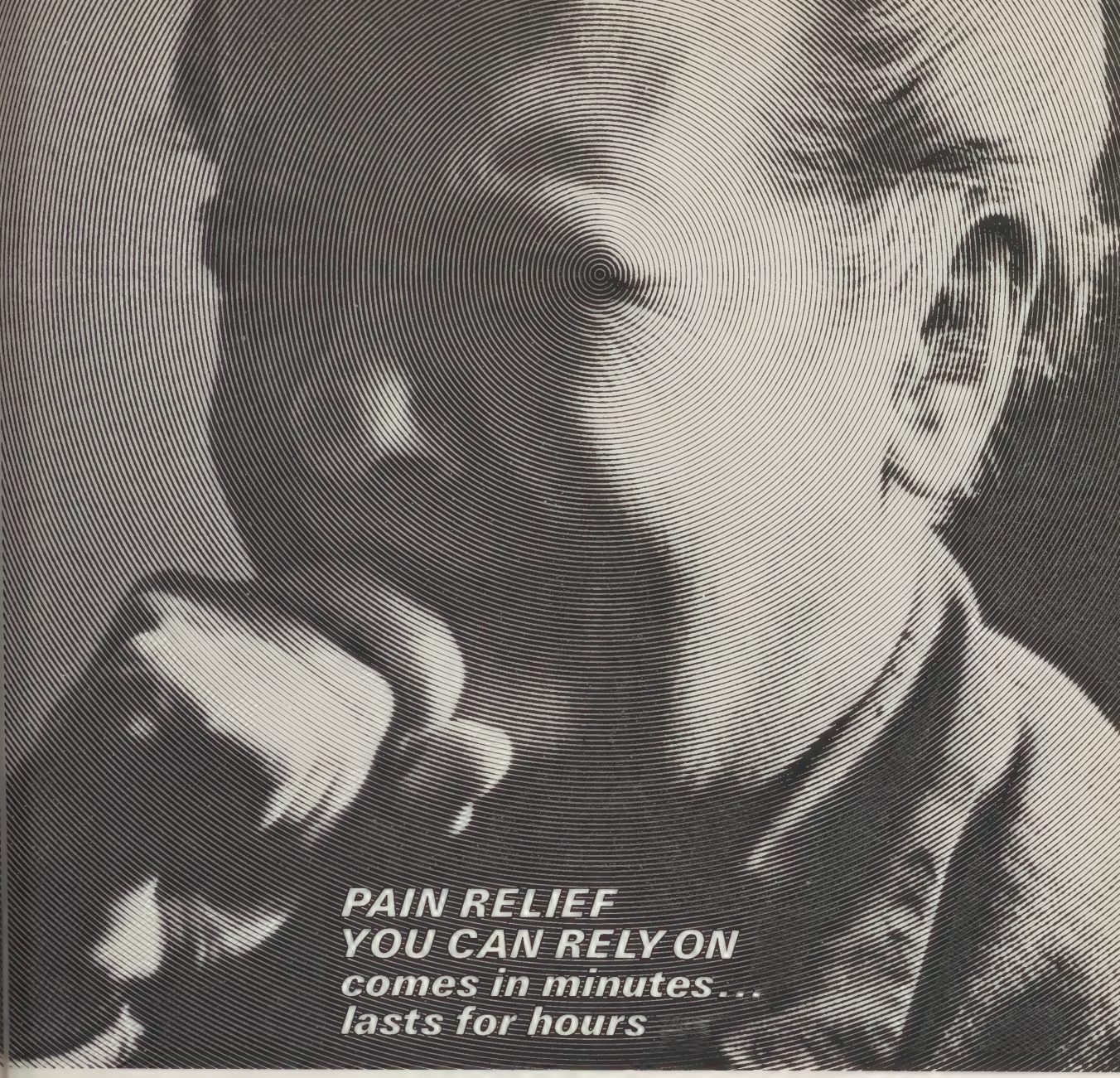
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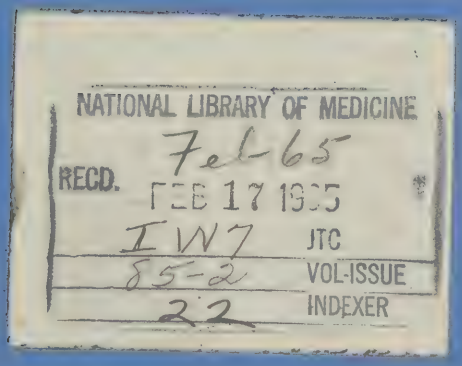
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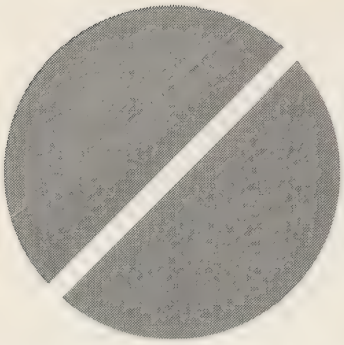
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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, *22*:527, 1964.

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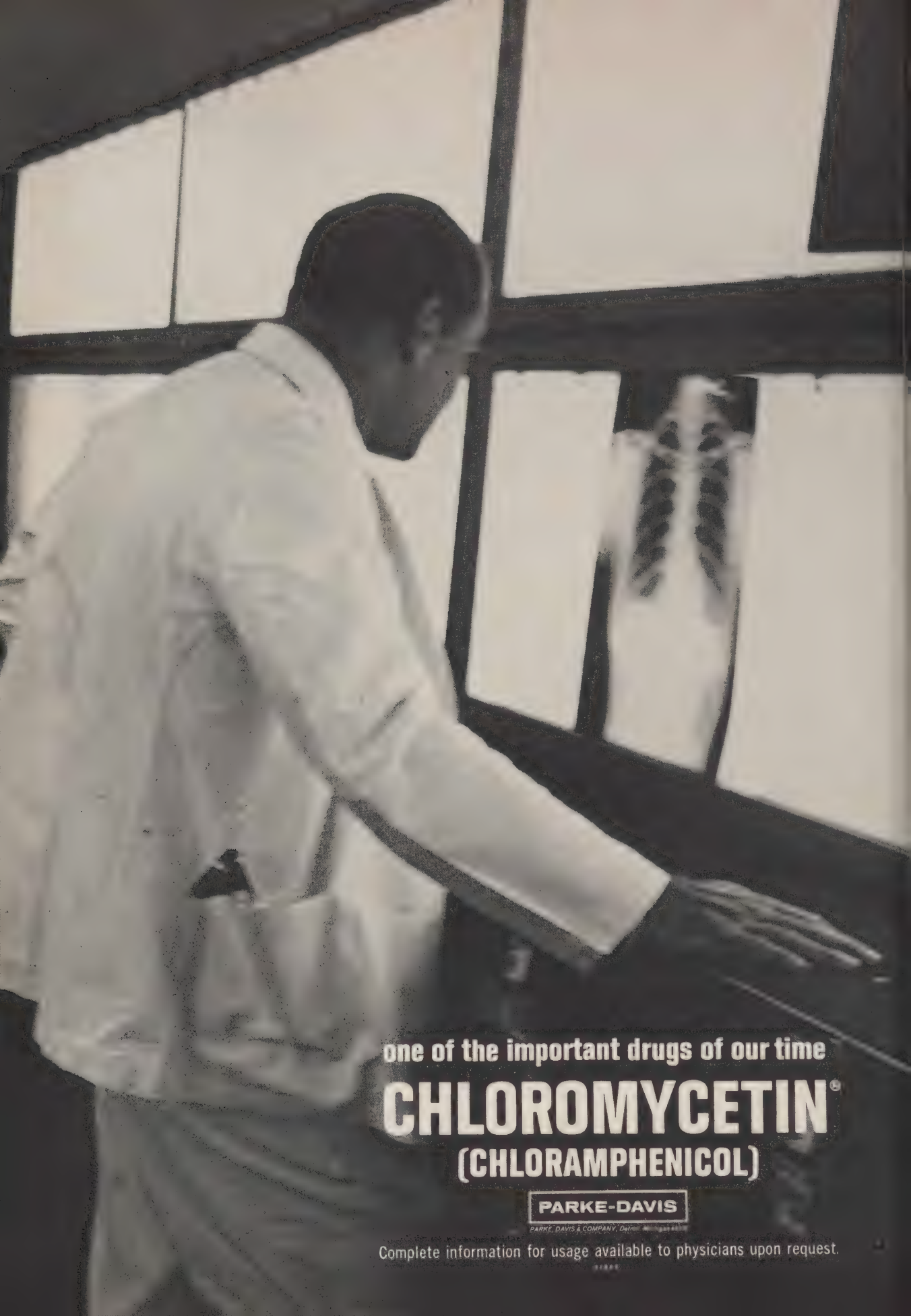
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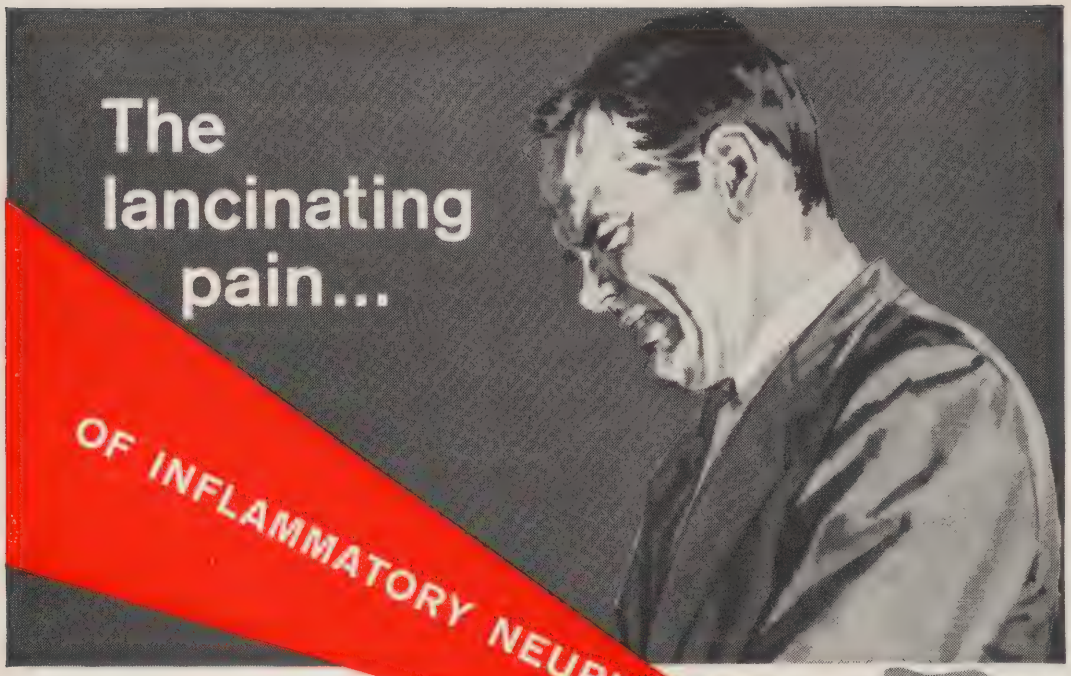
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COMING *in* *March*

Articles and features to be found in the next issue of THE JOURNAL-LANCET

The Editors of THE JOURNAL-LANCET are proud to announce the forthcoming publication of a 4-part series on "The Psychiatry of Presidential Assassination," by Donald W. Hastings, M.D., professor and head, Department of Psychiatry and Neurology, University of Minnesota Medical School, Minneapolis.

The first installment will appear in the March issue.

Dr. Hastings writes that of all of the possessions of Western man, government under law is perhaps the most painfully acquired. This means that each individual senses, or should sense, his moral obligation to settle his differences by legal processes and not by brute force and violence. He writes that "A resort to violence threatens the very foundations of our society and is abhorred by its members . . . . and violence is particularly abhorrent when it is directed at the highest symbol of our political system, the President of the United States."

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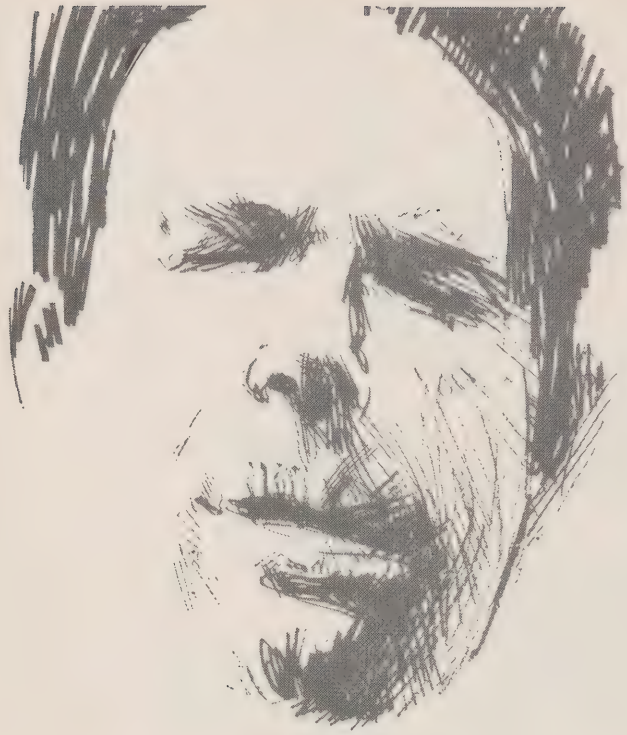
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Indications for the Use of Split- and Full-Thickness Skin Grafts

DONALD L. LAMB, M.D.

Fargo

THE FIRST unauthenticated accounts of free skin grafts were used by the Hindus in 1800 B.C. The first free graft reported in this country was in 1840 and performed by Jonathan Mason Warren in Boston. In 1886, Thiersch reported successful grafts with large split-thickness grafts, and in 1875 Wolfe reported the success he had with full-thickness grafts. Since these pioneer developments in the use of skin grafts, there have been many advances in the field. It is the purpose of this paper to define the types of free grafts now available, to explain the indications for the use of the various types of grafts, and to discuss some of the important technical features in the successful application of these grafts.

There are basically 7 types of skin grafts. They are the thin split-thickness, thick split-thickness, full-thickness, composite, flap, neurovascular or vascular island pedicle flap, and, still experimental, free island flap grafts.

Donor sites. The donor sites of these various grafts vary with the thickness of graft desired and the purpose for which the graft is intended. Thin split-thickness grafts are taken either with an electric dermatome or freehand with a No. 20 scalpel blade, if a small graft is desired, or with a long-bladed knife (Ferris-Smith or Blair), if a large graft is needed. Areas best suited to serve as donor sites for this type of grafts are the skin of the extremities (except over joints), the back, and the buttocks. The chest wall may be used but is made more difficult in thin people by the changing contour secondary to the underlying ribs. This problem in thin individuals can be partially circumvented by infiltrating the subcutaneous regions with normal saline. The skin of the abdomen is poorly suited for obtaining thin split-thickness grafts with an electric dermatome because of the lack of support beneath the skin, making it difficult to apply uniform pressure to the dermatome while cutting the graft. Thick split-thickness grafts are usually taken with a Padgett Hood or Riese dermatome. With this dermatome a 4×8 in. piece of skin can be cut at the desired thickness with less danger of cutting a thicker graft than anticipated. One of the faults of the electric dermatome is the tendency to cut deeper than desired when set at the thicker depths. When the manual dermatome is used, the abdomen, anterior and lateral thigh, and buttocks serve as the most satisfactory donor sites. When preparing these donor sites, a much larger area of skin should be prepared than the area that is desired to be taken as a graft. This is because the mechanical components of the dermatomes require freedom of movement. When grafts are taken off the buttocks or thigh, the moving portion of the blade should be aimed toward the distal portion of the extremity so as to prevent interference with the action of the dermatome. Thigh grafts are usually cut circumferentially, buttock grafts are taken vertically, and abdomen grafts are usually taken vertically, with care being taken to avoid removing skin

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from the inguinal fold, as there is a sudden change in thickness of abdominal skin at this level. Full-thickness grafts are usually taken with a scalpel. An elliptic incision is made through the dermis to include the desired amount of skin. One end of the ellipse is then taken with a hemostat and the dermis is separated from the underlying fat in a series of firm, but carefully applied, strokes with a sharp scalpel. For use on the extremities, the abdomen serves as the most satisfactory donor site. When full-thickness grafts are desired to cover defects of the face, the most satisfactory donor sites are the postauricular region and the supraclavicular region. In addition, for eyelid grafting, the upper lid serves as a satisfactory donor site for defects of the lower lid. Postauricular and upper eyelid grafts have the advantage of leaving no visible scar, whereas the supraclavicular grafts, particularly in females, leave a noticeable scar. The composite grafts most commonly refer to either earlobe grafts or, on occasion, when cartilage is desired, auricle grafts; the most common application is in reconstructive procedures of the nose.

Donor sites for flap grafts vary largely with the area to be covered. Most flaps of 2:1 ratio can be raised without a delaying procedure providing there is a subcutaneous artery and vein of sufficient size to support the flap. It is for this reason that positioning of the donor site of a flap is extremely important, and it is the reason why the thoracoacromion region, the lower lateral anterior thigh, and the chest and abdomen are desirable areas for obtaining flap grafts. These areas all have large subcutaneous vessels in a predictable location which makes application in a single stage possible. The most common donor site for the island pedicle flap is the temporal artery and vein and is used for reconstruction of either nasal defects or loss of eyebrows. Another common donor site for island pedicle flap is the neurovascular island pedicle flap of the finger in which the innervation and blood supply to an area of the ulnar side of a digit are preserved. This area is then transferred to a denervated or ischemic fingertip. Another example of an island pedicle flap is the Abbe-Eslander cross-lip flap, in which the labial artery serves as the nutrient vessel.

Care of donor sites. The care of the donor site depends on the type of graft obtained. The split-thickness grafts are best treated with an application of bismuth tribromophenate (Xeroform)-impregnated, fine mesh gauze directly over the donor site. After this, 1 of 2 courses can be followed: (1) The first course is the one most commonly used, and that is the liberal application of absorptive gauze dressing and a pressure bandage with either Kerlix or Kling followed by an Ace bandage. (2) The alternative course is to cover the bismuth tribromophenate with Telfa, place an absorptive dressing over it, and remove this dressing with the Telfa after four or five hours and begin the drying process of the bismuth tribromophenate at that time. If the first method is used, the dressing is usually removed down to the bismuth tribromophenate on the fourth or fifth day on the thin graft and the ninth or tenth day on the thicker site, and the donor site lamped appropriately. Lamping of donor sites is important, for it creates a dry environment in which the common organisms which produce infections of donor sites have difficulty surviving. The full-thickness donor sites are closed primarily in the abdomen. Subcuticular wire serves the purpose quite well. The eyelid and postauricular and supraclavicular regions are closed in the usual manner with sub-



Fig. 1. Postage-stamp, split-thickness grafts for covering of third degree burn defect



Fig. 2. Small area of third degree burn, three weeks posttrauma



Fig. 3. Small area of burn following primary excision and grafting



Fig. 4. Full-thickness, postauricular skin graft applied to full-thickness loss of skin of nose tip

cuticular catgut and interrupted cutaneous skin sutures. Subcuticular monofilament nylon (Dermalon) works particularly well in the eyelids. The donor site of the flap graft should always be covered with a split-thickness skin graft, as well as any exposed portion of the flap that is being used to carry from the donor to the recipient site. Ideally speaking, flap grafts should be completely healed by the use of split grafts, both on the donor site and the undersurface of the flap graft, at the time the flap is cut down.

Indications for the various types of skin grafts. Thin split-thickness grafts are primarly used to obtain coverage where little functional demand is placed upon them or when only a thin graft can be expected to take (Fig. 1). Examples where thin split-thickness grafts are indicated are burns, traumatic or contaminated wound closure, nonmoving surface cover, granulating wounds, and defects created by tumor extirpation when it is desired to be aware of any early recurrence of the tumor. The use of thick grafts to cover recently resected areas for tumor has a disadvantage of making detection of local recurrence difficult. However, thicker grafts are often indicated when one is confident of a curative resection. Thin split-thickness grafts will also take over freshly denuded bone but will not take over bone that has been exposed or contaminated.

The application of split-thickness grafts can be performed either by cutting them into small or postage-stamp size and placing them at appropriate intervals over the granulating base or can be laid down in large sheets. Generally speaking, the more epidermis that is transferred the better the functional result will be. It is important to cover joint surfaces with larger sheets of graft and to cover these early. The more ade-



Fig. 5. Bilateral syndactyly. Primarily flat coverage of thumb surface and index finger. Full-thickness skin graft to ulnar surface and middle finger

quate coverage of joints will enable improved function of the joint and decrease the discomfort of the patient. The amount of skin that is transferred in one operative procedure varies with the condition of the patient and the amount of donor skin available. Newer procedures for creating the smaller postage-stamp graft have been refined and are currently marketed by Zimmer, Inc. They have the advantage of producing a coverage over a maximum area with a minimum amount of donor skin, the disadvantage here being again the trading of scar epithelium for grafted epithelium. The advantages of early, prompt coverage must be weighed against the disadvantages of increased scar epithelium. Small areas of burn (less than 10% of body surface) can be handled quite expeditiously by primary excision of the burn area and split-thickness grafting (Figs. 2 and 3).

Thick split-thickness grafts, or grafts in excess of 0.015 in., are used primarily in releasing sec-

ondary burn-scar contractures, closing operative or relatively sterile wound defects, covering areas where growth is not anticipated, and, for the most part, covering a moving joint if there is a bed of fat. They are commonly used in the release of burn-scar contractures. The release of burn-scar contractures is indicated to improve function and to prevent Marjolin ulcers (squamous-cell carcinoma in a chromic burn-scar ulceration).

Full-thickness grafts are used when it is important to have dermal elements in the transplant. The 2 most important functions here are the presence of elastic fibers and the presence of the dermovascular bed which contributes to the vascular color of a skin graft. For resurfacing of defects over the face and nose (or the flush areas), full-thickness grafts taken from the postauricular and supraclavicular areas work the best, with respect to establishing a color match (Fig. 4). The rate of suntanning of various portions of the body varies tremendously, and the closer a donor site is to the recipient site the more likely the rate of tanning will be similar. In addition, a full-thickness graft establishes a circulation in the dermis which in turn more closely approximates the normal pink hue of the skin of the flush areas. With a split-thickness graft there is a tendency for the graft to become an undesirable white color, particularly if taken from a distant source. The second chief advantage of a full-thickness graft is the transplant of elastic fibers which allow stretching of the graft with growth. A most important application of this is in providing digit resurfacing in repair of syndactyly (Fig. 5). Flexion contractures of the digits should also be released by full-thickness grafts to aid in preventing subsequent redevelopment of the contracture.

Composite grafts are indicated when an additional substance other than skin is needed. Usually this includes fat, in the case of the earlobe graft, or cartilage, in the case of the auricular graft. The survival of a composite graft depends upon an early hookup of vessels of the dermal-to-dermal contact. This can be expected to produce survival of about 7 to 9 mm. of skin. Therefore, if a circular-type defect is involved, survival of grafts exceeding 2 cm. in diameter is the exception rather than the rule. Survival of grafts under 2 cm. in diameter can be expected to occur in a large number of cases. They are most commonly used in the reconstruction of the columella and alar defects and have also been used to correct lip and eyebrow defects (Fig. 6).

Mechanism of survival. The mechanism of how a graft survives is broken down into 2 phases.

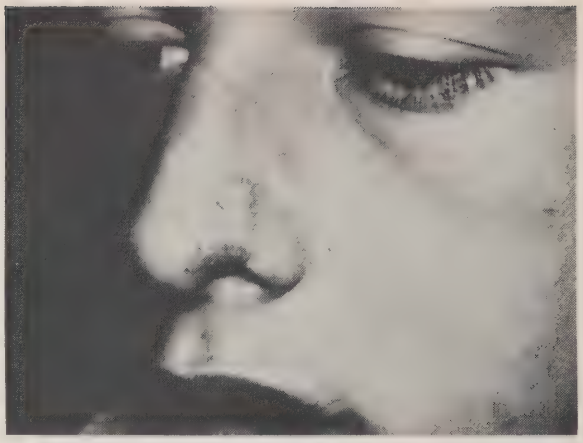


Fig. 6. Earlobe composite graft, left ala

For the first three days a type of circulation called "plasmatic" circulation is in effect. This is in some ways analogous to the manner in which a dry sponge soaks up water. The open capillaries are gradually filled with serous fluid which escapes into the space between the graft and the recipient site. As early as the first twenty-four hours following dermal-to-dermal contact, and a slightly later time in the undersurface of the graft, a capillary hookup occurs. After three days this hookup is well established, and the nourishment of the graft then occurs primarily through the flow of the capillary network. Any factors that interfere with either the plasmatic circulation or the capillary hookup may result in the loss of the graft. In the case of the full-thickness grafts, it is important to place the grafts in approximately the same tension as the graft occupied in vivo. Stretching the full-thickness graft to cover the defect or allowing it to shrink tends to interfere with the plasmatic circulation, in that the capillaries are compressed either as a result of stretching or as a result of



Fig. 7. Plaster-of-paris immobilization device for cross-thigh flap

the unopposed contractility of the elastic fibers. Factors such as an ischemic recipient site or mechanical interference to the growth of capillary buds into the graft tend to compromise the survival of the graft. The most common mechanical interference of the capillary growth is the presence of postoperative hematoma. Perhaps second most common is postoperative infection. It is for this reason that absolute hemostasis of the recipient site is important. The sterility factors are obvious. It is important to apply pressure during the early phases of a skin graft to decrease the likelihood of hematoma formation and to help in the immobilization of the skin graft. Immobilization of the part in order to prevent any shearing action of skin graft on recipient site is of extreme importance so as to prevent a shearing off of the recently established capillary hookup, which in turn will create subgraft hematomas that will prevent further capillary hookup. It is nearly always indicated to carefully splint or, preferably, cast skin grafts to the extremities. Where casting is impractical, such as in the axilla and cervical region, carefully applied tie-over, bolster-type dressings and bulky pressure dressings are used to achieve the same end.

Flap grafts. Indications for flap grafts arise when past experience has shown that split- or full-thickness grafts are either impractical or unsuitable. Usually what is required is a fat cushion to prevent recurrent trauma to the skin, particularly where bone is being covered. Other indications are when tendon grafting must be performed through an operative or traumatic defect or when the recipient bed is unsuitable to receive a graft. When defects of body cavities are created and need coverage, flap grafts must be the next resort. Healed areas of osteomyelitis, auricular defects, lip defects, deep burns in the vicinity of tendons, and split-thickness graft coverage over bone are other examples of where flap grafts are necessary. The most important feature of flap transfer is the careful planning of the flap. The donor site must be carefully selected so that the subcutaneous area contains blood vessels of suitable size to support the proposed flap. The flap must be cut of sufficient size, the most common mistake in this area being to cut the flap of insufficient proportions to cover the defect to be created. The second most important feature is a broad application of the flap so as to reconstitute secondary circulation over as large an area as is possible to improve the ratio of the flap during detachment. Whereas the initial flap can be well supported on a 2:1 ratio, the reverse is commonly necessary when cutting down the flap graft. "Severance slough" is a very common entity and can be largely prevented by the proper application of the flap and by subsequent proper delay in the process of cutting down the flap on the eighteenth to twenty-first day. Another extremely important feature in the successful completion of a cross extremity flap is the establishment of adequate immobilization. The slightest degree of torsion possibly can result in edema on the base of the flap with subsequent loss during application. It is for this reason that extensive plaster and splint apparatus are utilized and the joints must be maintained in a comfortable position and in a position that requires no effort on the part of the patient (Fig. 7). The least amount of muscle effort to maintain a position results in a muscle spasm which patients find intolerable after a period of a few days. It is often necessary to make the three-week compulsory period of flap attachment easier by the use of mild tranquilizing agents. During the early phases of the flap transfer, the flap must be watched extremely closely. At the

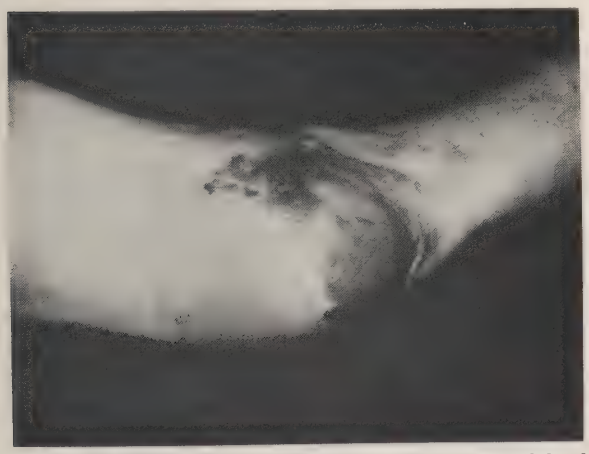


Fig. 8. Inadequate split-thickness skin coverage of heel

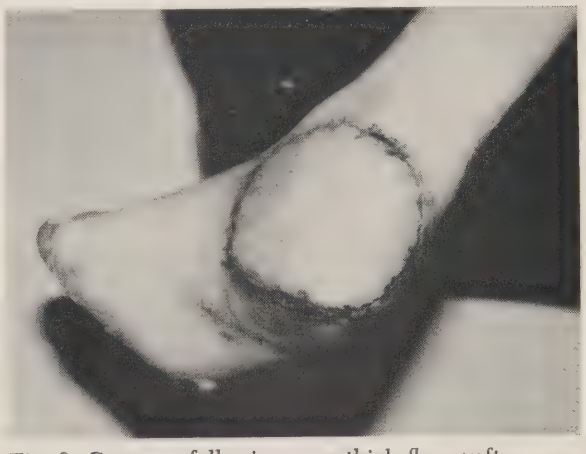


Fig. 9. Coverage following cross-thigh flap graft

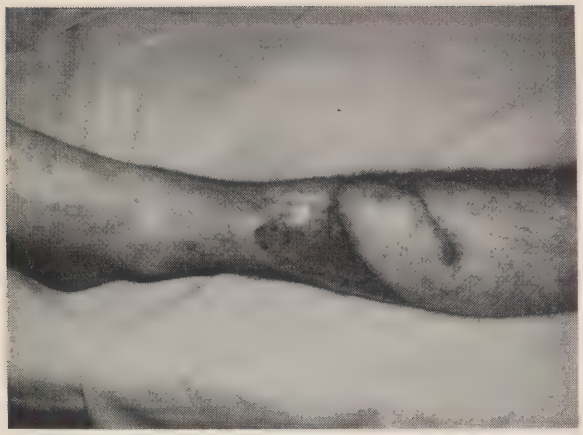


Fig. 10. Adjacent rotation flap with split-thickness grafting of donor site

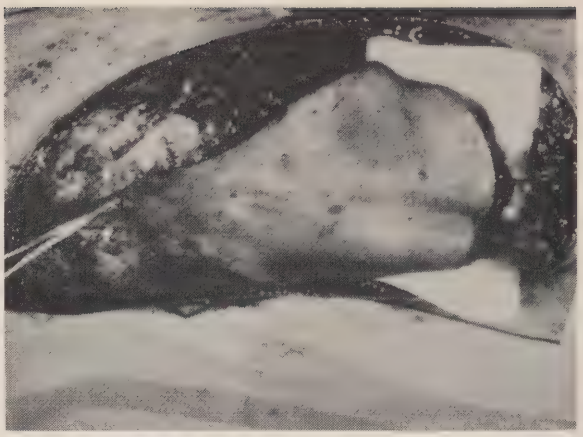


Fig. 11. Experimental island flap based on both caudal epigastric artery and vein of dog

first sign of color changes of the skin, the position should be checked. If the flap appears blue or engorged, the base of the flap should be placed in a dependent position. In contrast, at the first sign of ischemia the flap should be positioned so as to put the base of the flap higher than the rest of the flap to augment arterial inflow. Prompt and early positioning of flaps can thus prevent serious complications and achieve desired results (Figs. 8 and 9). The use of intravenous heparin, massage, and local hypothermia also have their place in the treatment of flaps with compromised blood supply.

The neurovascular island flap is very useful in restoring types of sensation to denervated fingertips and also to restore blood supply to an ischemic digit. Adjacent rotation flaps are used to cover small defects in the well-nourished extremity and are particularly useful in covering decubitus ulcers, so prevalent in the paraplegic population (Fig. 10).

Free island flaps is a new concept made possible through the use of microsurgical apparatus. It is a flap in which a large island flap of skin is created, based on a single artery and vein. The artery and vein are transected and resutured into a suitable artery and vein in the recipient site. This form of flap successfully performed would make unnecessary the compulsory three-week waiting in uncomfortable positions with the currently used methods of flap transfer. The procedure is still experimental and has been performed with only limited success in animals. It is to be anticipated with refinements in microsurgical techniques that this method of flap transfer will some day be feasible. In dogs, large island flaps have been shown to be supported with small arteries and veins, and the division and the anastomosis of these vessels is possible. Flaps have been shown to survive up to three days following this technique (Fig. 11).

SUMMARY

The types of skin grafts currently available have been defined with their indications. The importance of the application of certain basic surgical principles as they apply to skin grafting has been emphasized. A plea for the proper selection of the type of graft based upon suitability of recipient site and anticipation of future function and the availability of donor skin is made.

The Natural History of Tuberculosis in the Human Body.

VII. Prognosis Among Children of Six to Seventeen Years Old with Previous Clinical Disease on First Examination

J. ARTHUR MYERS, M.D.
Minneapolis

In May, 1921, Dr. F. E. Harrington, Commissioner of Health, Board of Public Welfare and Director of Hygiene of the Minneapolis Board of Education, established a school and clinic for tuberculous children in a building donated by the G. R. and F. W. Lyman families. The building had been constructed on the grounds of the old family homestead, hence the institution was named Lymanhurst. The purpose of this project was to find and treat, or recommend treatment for, children throughout the city who had clinical tuberculosis, and to conduct research on tuberculosis among children. It was realized that even a short segment of the natural history of tuberculosis in the human body had not been determined because no one had made extensive and prolonged studies to establish late prognostic baselines of children who became invaded with tubercle bacilli.

A medical staff was organized which began with two members but was extended to 98 including experts in all the specialties of the medical profession. Each expert including internists, surgeons, dermatologists, orthopedists, physiologists, neurologists, cardiologists, pediatricians, and roentgenologists was given the opportunity of conducting special investigations in his field on the 160 children enrolled in the school and a large number in attendance at the clinic. These staff members who donated their time and work produced numerous manuscripts from their research, many of which were published.[1–9] As the years passed an additional 202 physicians contributed to support of the project by reading papers before staff meetings, and so forth.[10]

One of the main functions of the organization was to conduct extensive and intensive epidemiological studies. For every child who, at the clinic or elsewhere, was found to react to tuberculin a careful search was made for the person or persons with contagious tuberculosis to whom he had been exposed. Moreover, whenever a clinical case (nearly always an adult) was reported to the health department an extensive search was made for the persons, especially children, who had been in contact with this individual. They were tested with tuberculin. Large numbers of children were found to react, which was considered proof that they had been invaded with tubercle bacilli.

Most of the epidemiology was done by public health nurses of whom there were nearly always more than 20 devoting the greater part of their time to this work. Between 1921 and 1941, in fact, 68 public health nurses in the Civil Service participated and 21 additional nurses were assigned to this activity for a part of the duration of the Works Projects Administration. There were also 22 public health school nurses who were active in this program. In addition to this large

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public health nursing service the institution was well supplied with excellent secretarial and clinical workers. This was by far the largest and most intensive epidemiological study on tuberculosis made before or since in any area with similar population.[10]

Between 1921 and 1941 more than 19,000 children were examined at the Lymanhurst Institution. They ranged from infancy through the senior year of high school. Many of them have had frequent periodic examinations over the years to the present time and have constituted the basis for extensive research on the natural history of tuberculosis in the human body. A number of papers have been published in national and international medical journals and more are in the making. Tracing these former Lymanhurst children throughout the years has been a monumental task, particularly the girls whose names have been changed through marriage. Moreover, it is an extremely expensive undertaking and requires patience that at times is almost unbelievable. Nevertheless, it is the only way the natural history of a chronic lifetime disease can be revealed.

Observations on these children while they were still of school age and subsequent follow-up between 1921 and 1963 revealed facts concerning the natural history of tuberculosis not previously known. Some of the well documented evidence was diametrically opposed to theories, speculation, and opinions that had long been accepted as facts. Considerable controversy was waged by those who had so long held beliefs for which proof was lacking. Space permits mention of only the following few items which were thoroughly demonstrated by longitudinal studies.

ONLY TUBERCULIN REACTORS DEVELOP CLINICAL DISEASE

In 1921, and for a few years thereafter, the tuberculin reaction was believed to indicate the presence of dependable immunity with little or no danger of reactors developing clinical tuberculosis. However, longitudinal observation on the same children as they passed into adulthood revealed that it was only the tuberculin reactors who developed clinical tuberculosis in the lungs and extrathoracically.

TUBERCULIN REACTOR REGISTER ESTABLISHED

These observations were made on a sufficiently large number and over a long enough time to leave no doubt that past emphasis had been placed on the wrong group, namely non-reactor to tuberculin children. Time and effort had been expended on those children who had not been invaded with tubercle bacilli while tuberculin reactors as they attained adulthood developed clinical disease and disseminated tubercle bacilli among their associates. Learning that only persons who at the moment are tuberculin reactors or subsequently become so develop clinical tuberculosis greatly facilitates the solution of the problem in any area. This observation was made in the late 1920's. In 1930 the Commissioner of Health of the City of Minneapolis requested that physicians report not only frank clinical cases of tuberculosis but also all tuberculin reactors, even though the reaction was the only evidence of the presence of tuberculosis. The reports of the reactors who had no demonstrable clinical tuberculosis were filed separately from those with clinical disease, first to be used in epidemiological activities—that is, in an attempt to locate unknown or unsuspected communicable cases—and secondly, to arrange for periodic examination of all adult reactors at the time of the test, and of all reactors among the children as soon as they attained adulthood. This seemed an extremely drastic step because prior to this time most everyone had used the word "tuberculosis" synonymously with the word "consumption." That is, no one was thought to have tuberculosis until clinical lesions were seen when the disease had entered the last lap of its natural history in the victim's body. This new venture met with some opposition as has been true with every innovation in medicine. Indeed, in 1933 a committee of the Minnesota Trudeau Society (later called the Thoracic Society) recommended that first infection type of tuberculosis as manifested by the tuberculin reaction be reported to the health department by physicians throughout the state. This recommendation was lost by almost a unanimous vote of the society. However, it was extremely gratifying to note that another committee was appointed which met in 1941 and made the following recommendations:

1. That all reinfection and extrapulmonary tuberculosis be reported to the State Board of Health.

2. That anyone with primary infection as demonstrated by tuberculin reaction with or without clinical or laboratory findings should be reported as such in order to allow for proper epidemiological work including examination of all intimate contacts but not to be counted as cases of tuberculosis.

3. That both groups be reported on the same form.

This was unanimously adopted, however, not until eight years after the first infection type of tuberculosis as demonstrated by the tuberculin

reaction was considered reportable by the health official. Apparently the 1930 register for tuberculin reactor children was the first of its kind in this country.

TUBERCULIN TESTS ADMINISTERED BY NURSES

In the 1920's physicians approved administration of tuberculin tests by private office nurses, but they were reluctant to recommend that nurses administer this test elsewhere. When Lymanhurst was established 6 full-time nurses were regularly on duty to give care to the children in the school and in the ward. These nurses participated in the tuberculin testing. In 1931 Dr. W. L. Rathbun, Medical Director, Chautauqua County Sanatorium, New York, delegated extensive tuberculin testing to public health nurses with most satisfactory results, both from the standpoint of administration and interpretation. Learning of this demonstration F. E. Harrington, Commissioner of Health, Minneapolis, instructed two public health nurses in tuberculin testing. His demonstration was also so satisfactory that soon nearly all tuberculin testing in the health department was done by nurses. This was a fine forward step as the volume of tuberculin testing was so great as to require the work of both nurses and physicians.

PRIMARY TUBERCULOSIS EXCEEDINGLY BENIGN

In 1921 primary tuberculosis was generally believed to be exceedingly destructive particularly in young children and in teen-age girls and boys. It was spoken of as "infantile tuberculosis"—a term synonymous with death.

Many persons expressed the opinion that in infancy and early childhood the human body has exceedingly "high susceptibility and low resistance" to tubercle bacilli. Inasmuch as in the early part of this century most of the tuberculosis mortality among children, from birth to four years, was due to acute, highly fatal forms of the disease, which usually were ushered in by sudden onsets with no previous manifestation, it was thought that these conditions were primary.

After safe methods of administering tuberculin became available in 1907 and 1908, and it was believed a reaction indicated presence of tuberculous infection, it was thought that any apparently well child who reacted to this test during the first year of life would soon die from "infantile" tuberculosis, and that at least half of those who reacted to the test between the ages of 1 and 2 years were doomed.

However, in 1920 search of the literature revealed that practically all that had been said and written was a matter of opinion since no documented study was found to justify a conclusion.

In the series of acute clinical cases reported, rarely had there been at attempt to determine how many infants and young children were infected with tubercle bacilli in the areas from which the ill ones originated. Our observations revealed that a very small percentage of infected infants and young children die from acute forms of tuberculosis such as meningitis and miliary dissemination. It was shown that the primary invasions with tubercle bacilli resulting in primary pulmonary tuberculosis complexes almost never become significantly clinical.

The reason that the lesions of primary complexes are so benign is that they start to develop on tissues that have not been sensitized to tuberculoprotein. Therefore, nature proceeds to wall off the tubercle bacilli just as she does inanimate material of the particulate type such as silicon-dioxide particles. Hence, the destruction from the primary type of tuberculosis per se is extremely minute and practically never causes significant prolonged incapacity.

CLINICAL TUBERCULOSIS DUE TO REINFECTIONS (USUALLY ENDOGENOUS)

Clinical disease including the acute forms like meningitis and miliary dissemination as well as chronic lesions of the lungs, bones, and joints is due to endogenous reinfections. These come about by nature treating the lesions of the primary tuberculosis complexes paradoxically. That is, after going to the trouble of walling them off she breaks down the walls and liberates the tubercle bacilli that have been so well encapsulated. This may occur early in the course of the evolution of the lesions of primary complexes and result in meningitis, pneumonia, miliary dissemination, pleuritis, pericarditis, peritonitis, and synovitis. However, the percentage of tuberculin reactor children who develop these acute forms is relatively small. The great destruction in the human family comes much later when nature paradoxically resorbs the osseous, calcific, and fibrous capsules thus liberating tubercle bacilli. While the lesions of the primary complexes are developing, the tubercle bacilli liberate tuberculoprotein which sensitizes the tissues throughout the body. This sensitivity converts tuberculoprotein into a violent poison to tissues. As long as the tubercle bacilli are "locked up" in capsules no destruction or ill health occurs. However, if nature paradoxically liberates them they promptly set up specific inflammatory processes as the protein kills cells and tissues with which it comes in contact. From these endogenous reinfections clinical tuberculosis starts to develop.

CHRONIC FORMS OF PULMONARY TUBERCULOSIS USUALLY RESULT FROM LONG-STANDING INFECTIONS

It soon became evident from our longitudinal observations that the bulk of the "break-downs" from chronic clinical pulmonary tuberculosis are the result of long-standing infections and occur among persons whose tissues have been sensitive to tuberculin for years or even decades.

A child may be invaded with tubercle bacilli today with no external manifestation and there is no way of detecting the condition for three to seven weeks. Then allergy has developed so the individual's tissues react to tuberculin. At that time there is at least a 95% chance that the x-ray film of the chest will reveal no abnormality in the lungs or hilum region. In most cases, if the tuberculin test were not administered the individual would join the billions who have had the same condition without having been aware of its presence. However, this same child may grow to adulthood, attain the age of 40 years and develop chronic endogenous reinfection type of pulmonary tuberculosis from the progeny of the tubercle bacilli which entered his body when he was a child. The development of clinical disease at that time is not related to where he works or his occupation. It is unfortunate that this information has not been generally disseminated. Unfortunate because lack of information results frequently in terrible injustice to the individual and to his employer. When the symptoms appear he is likely to blame his work or something associated with it, such as a whiff of chlorine gas, silica dust, or long working hours. He honestly believes that his employer is responsible and therefore should pay for the entire disability. The attorney who presents his case is equally uninformed and so are members of the jury, the judge, and the industrial commission referee. Therefore, his chances of being compensated unjustly are well nigh 100%. The criticism is not directed to those involved in the legal proceeding but to our own profession and our allies, including tuberculosis organizations, for not having disseminated the well-known information—that the person responsible for this man's breaking down was the one who infected him as a child. It may have been his own mother.

CHANGE OF DEFINITION OF TUBERCULOSIS IMPERATIVE

In the 1920's when it was thoroughly proved that only persons who react to tuberculin subsequently develop clinical tuberculosis, it was obvious that the definition of tuberculosis should be changed. Prior to that observation this word always referred to clinical disease while persons who reacted to tuberculin, with no other evidence of tuberculosis, were said to be infected but not diseased. In other words, it had not previously been recognized that within an hour after tubercle bacilli invade the human body microscopic areas of disease have started to develop, after which the individual has tuberculosis.

DIAGNOSIS BY ROENTGENOGRAPHIC SHADOWS ALONE OPPOSED

In the early 1920's it was shown that x-ray film inspection of the chest often reveals shadows of lesions which are not found by other phases of the examination. This procedure was recommended as a routine part of every examination. However, it was observed that no disease casts an x-ray shadow all its own which differentiates it from other diseases. Other diagnostic procedures are necessary to determine the etiology of the area of disease casting the shadow.

When our campaign for the extensive use of x-ray film inspection of the chest began, it was inconceivable to us that anyone would advocate that the x-ray film could be used as a final diagnostic agent. We were under the impression that all physicians knew that even pathologists cannot diagnose etiology from naked eye inspection of gross lesions and that many diseases cast identical shadows on x-ray films. However, as soon as routine x-ray film inspection of the chest became well popularized, a group, contending that diagnoses could be made from shadows only, sprang into existence. This has proved to be one of the most serious handicaps of the tuberculosis control movement, since those who accepted it completely ignored the tuberculin test and other phases of the examination. Many a person was placed on treatment for tuberculosis whose original x-ray shadow was cast by resolving pneumonia, fungus disease, malignancy, congenital cystic disease, abscess, and bronchiectasis.

All of this was well known before the overenthusiasm developed throughout the country for mass x-ray surveys. Nevertheless, the well documented evidence against such a procedure was ignored by such survey promoters. No one doubts that mass x-ray film surveys brought to light shadows of some lesions which proved to be tuberculous, but they missed all of the people who had tuberculosis in whom gross lesions had not evolved in their lungs. The mass chest x-ray survey therefore is not economically sound. However, it took more than a decade on the mass x-ray survey tangential excursion before the error was generally recognized, and still longer before most workers returned to the far more effective and economical procedure of x-ray film

inspection only of chests of tuberculin reactors.

Our roentgenologic observations over the period of 1921 to 1931 never revealed evidence of disease of clinical significance in the lungs of a child who did not react to tuberculin. Therefore it was recommended and practiced for approximately a third of a century that x-ray film inspection of the chest be limited to persons who react to tuberculin. During the same period it was shown that films of the chests of children under the age of 12, although they react to tuberculin, reveal evidence of significant lesions so rarely that it is poor economy to make them unless a special indication exists.

ROENTGENOGRAPHIC INSPECTION OF CHESTS OF TUBERCULIN REACTORS OVER 12 YEARS OLD IMPERATIVE

From the age of 12 every child and adult who reacts to tuberculin should have x-ray film inspection of the chest periodically. While x-ray film inspection of the chests of children who have recently become tuberculin reactors under the age of 12 are practically useless, the x-ray film constitutes by far our best diagnostic procedure, if and when the endogenous reinfection type of clinical pulmonary tuberculosis evolves. This evolution is slow and usually "silent" for two or three years. During this time periodic x-ray film inspection locates the evolving lesions as soon as they become macroscopic and have sufficient consistency to cast shadows. It is in this manner that lesions can be found before they cause symptoms, before they are communicable, and when they can be treated successfully.

LESIONS AMONG CHILDREN FROM 6 TO 17 YEARS OF AGE

It has been observed in various parts of the world that the reinfection clinical types of tuberculosis are relatively rare among children from 6 to 12 years. In fact, the morbidity and mortality rates in this age group are the lowest of any period in life's span. There has been racking of brains to learn why individuals from 6 to 12 have such "low susceptibility and such high resistance" to tubercle bacilli. However, our observations have revealed that during this period tubercle bacilli are far more active than morbidity and mortality would indicate. Many children who had been infected earlier in life entered this period and many more became invaded during the ages of 6 to 12. A survey made in 1926 in certain selected schools throughout the city revealed that slightly more than 20% of the 6-year-old children were harboring tubercle bacilli. This increased to 60% at the age of 12. By 1954 these figures had been reduced to 1.2 and 5.2 respectively.[11] We became convinced that as long as any child enters this age period harboring tubercle bacilli or becomes invaded during this period, a tuberculosis problem exists.

Among the 19,045 children examined at the Lymanhurst School and Clinic there were only 31 between the ages of 6 and 12 who had been previously treated for tuberculosis and reported periodically for reexamination, or who had clinical tuberculosis first detected at the time of our original examination. To this group of children has been added 15 from a follow-up study of children who were found to be tuberculin reactors between the ages of 13 and 17 but who previously had clinical tuberculosis.

The 46 children found to be reactors to tuberculin between the ages of 6 and 17 are being presented to show types of clinical lesions which had developed before we first saw them, and also to demonstrate immediate and remote prognosis. In reading these brief case histories it will be observed that a sizable number had tuberculosis of the skeletal system which had been treated quite early in life.

EXTRATHORACIC LESIONS IN GIRLS

There were 19 girls with extrathoracic tuberculosis as follows:

A 6-year-old girl was first seen in 1930 when she reacted to tuberculin. Tuberculosis of the left hip had been treated in 1927. No further evidence of clinical disease had been found. She is now 39 years old and has been followed thirty-three years.

In 1927 a girl of 7 reacted to tuberculin. In 1922, when she was 2 years old, she was in a sanatorium because of tuberculosis of the left kidney. Nephrectomy was performed. In 1938, when she was 18 years old, an area of disease appeared in the left lung which was treated successfully. She has since remained well and is now 42 years old. She has been followed thirty-five years.

An 8-year-old girl was first seen in 1936 when she reacted to tuberculin. She had tuberculosis of the right ankle bones and was treated in a sanatorium from 1932 to 1934, and for one year in 1939. There has since been no evidence of clinical disease. She is now 44 years old and has been followed thirty-eight years.

A girl was first seen at the age of 8, in 1921, when she reacted to tuberculin. She had tuberculosis of the left hip joint which had been treated in a cast at home from the age of about 4 to 8. She has since had no evidence of clinical

tuberculosis. She is now 50 years old and has been followed forty-two years.

At the age of 8 a girl reacted to tuberculin when first examined in 1938. She had been in a sanatorium from 1935 to 1937 for treatment of tuberculosis of the right hip joint. In 1941 a cast was applied and continued as indicated. She had no further evidence of clinical tuberculosis. She is now 33 years old and has been followed twenty-five years.

Another girl of 8 was first examined in 1928. She reacted to tuberculin. Tuberculosis was present in her left hip joint. This was treated surgically in a sanatorium and she was discharged in 1933. She has remained free from clinical tuberculosis. She is now 43 years old and has been followed thirty-five years.

At the age of 8, when first examined in 1935, a girl reacted to tuberculin. Tuberculosis was present at the proximal end of the left femur. She was readmitted in 1939 with marked destruction of the left hip joint. Further surgery was performed. She was discharged in 1946. There has since been no evidence of progressive tuberculosis. She is now 35 years old and has had twenty-three years of follow-up.

In 1922, when a girl of 10 was first examined, she reacted to tuberculin. At age 2 she had a diagnosis of tuberculosis of the right hip joint. She was in a sanatorium a total of about 9 years. There has been no evidence of clinical disease since discharge. She is now 51 years old and has been followed forty-one years.

When a girl of 12 was examined in 1930 she reacted to tuberculin. She then had tuberculosis of the seventh to eleventh dorsal vertebrae which was being treated by an orthopedic surgeon. She was admitted to a sanatorium with paravertebral abscess and empyema. She died in 1939 at the age of 21, having been followed nine years.

When first examined in 1927 a girl of 12 reacted to tuberculin. At the age of 2 tuberculosis was found involving mid-dorsal vertebrae. She was on a Bradford frame for two years. No evidence of clinical tuberculosis has since appeared. She is now 47 years old and has been followed thirty-five years.

A girl of 12 was first examined in 1923 when she reacted to tuberculin. She had tuberculosis of the left knee and was treated in a hospital for crippled children. There apparently were fibroid deposits in the apex of her right lung. In 1925 there was an increase in extent of the disease in this area. In 1926 this appeared the same but there was also a small area of disease in the apex of the left lung. Later in that year and again in 1927 the disease had definitely extended in both lungs. She was admitted to a sanatorium in 1929 and was discharged in 1934. She was readmitted to the sanatorium in August 1937 and discharged in December 1937. There has been no further evidence of clinical disease. She is now 52 years old and has been followed forty years.

In 1939 a girl 12 years old reacted to tuberculin. She had tuberculosis of the left auxiliary lymph nodes. She was admitted to a sanatorium in December 1939 and discharged in May 1941. No evidence of clinical disease has since appeared. She is now 35 years old and has had twenty-three years of follow-up.

In 1930 a girl of 12 was first examined when she reacted to tuberculin. She had tuberculosis of the skin of her hands and calves of her legs. She was treated in a sanatorium and the disease was classified as arrested in 1934. There has since been no evidence of reactivation or formation of new clinical lesions. She is now 45 years old and has been followed for thirty-three years.

When a girl of 13 was first examined in 1927 she reacted to tuberculin. No evidence of clinical disease was found in her chest. However, she had extensive destruction of the middle and lower dorsal vertebrae with marked kyphosis. This disease was known to be present in 1922. There was no other evidence of clinical tuberculosis. She died from a cardiac condition in 1952 at the age of 37, after twenty-five years of follow-up.

A girl of 13 was first examined in 1936 when she reacted to tuberculin. She had been in a sanatorium with tuberculosis of the left lung, and was discharged in 1935 when her disease was classified as arrested. While in the sanatorium she also had a diagnosis of tuberculosis of the right astragalus and ankle joint, which was treated surgically. She was readmitted to the sanatorium in January 1937 and discharged in August 1937 when her pulmonary disease was classified as arrested. She has remained well. She is now 40 years old and has been followed twenty-seven years.

A girl of 13 reacted to tuberculin when first examined in 1931. There was no evidence of pulmonary disease. She had been admitted to a hospital for crippled children because of tuberculosis of the right knee joint in 1924, and was discharged in 1926. She was readmitted in August 1930 because of a draining sinus, and was discharged in March 1931. She was last seen in 1940 when she had a perfect fusion of the right knee with two inches of shortening in the right leg. She was then apparently in excellent health.

A girl of 14 was first examined in 1928 when

she reacted to tuberculin. Her lungs appeared clear but there was thickening of the pleura over the base of the right lung. On the original examination she had involvement of the lumbar vertebrae, with kyphosis. She died in 1933 of chronic glomerulonephritis and terminal pneumonia at the age of 19, having been followed five years.

A girl of 14 reacted to tuberculin when first examined in 1930. Her lungs appeared clear. She had a diagnosis of tuberculosis of the left hip at the age of 4. No surgery was necessary. She has since been in good health but is slightly lame. She is now 47 years old and has been followed thirty-three years.

A girl of 15 was first examined in 1930. There was no history of exposure but she reacted to tuberculin. Calcium deposits were present in the right hilum region. She had extensive disease involving the third to the ninth dorsal vertebrae with kyphosis. She was last seen in 1937 when she was feeling well, but refused to be examined in 1941. She died from acute cor pulmonale, chronic bronchitis, and bronchiectasis in 1954 at the age of 39 with twenty-four years of follow-up.

Of the 19 girls who had extrathoracic tuberculosis, 12 survived. Of the 4 who died the average age at death was 29. Only 1 was due to tuberculosis. The present ages of the 11 still living range from 33 to 52 years with an average of forty-three and one-tenth years. They have been followed four hundred sixty-three person-years. One has not been traced since 1940 when she had been followed nine years.

EXTRATHORACIC LESIONS IN BOYS

There were 12 boys with extrathoracic tuberculosis as follows:

On first examination in 1925 a boy of 7 reacted to tuberculin. He had marked kyphosis of the dorsal vertebrae. This disease was first detected at 2 when chiropractic treatment was administered. He is now 45 years old and has been followed thirty-eight years with no further evidence of clinical disease.

On first examination in 1924 a boy of 7 reacted to tuberculin. He had a diagnosis of tuberculosis of the right knee joint at the age of 17 months. In 1941, aside from lameness, he was found to be in good health. He has not been located since 1941.

A boy of 7, when first examined in 1933, reacted to tuberculin. He had been treated in a sanatorium from July 1929 to April 1933 for tuberculosis of the sixth and seventh cervical vertebrae and tuberculous cervical adenitis. He was in the sanatorium again for eight months in 1935. In August of that year his disease was classified as apparently arrested. There has been no further evidence of clinical disease. He is now 37 years old and has been followed thirty years.

At the age of 8, when examined in 1922, a boy reacted to tuberculin. He had marked kyphosis resulting from tuberculosis of the ninth through the twelfth thoracic vertebrae which had been treated when he was 2 years old, in 1916. He is now 48 and has had forty years of follow-up.

A boy of 9, in 1922, reacted to tuberculin. In 1919, at the age of 6, he had been treated for tuberculosis of the right knee joint. He still had limitation of motion of that joint. He remained apparently well and active until 1932 when his private physician reported far advanced bilateral pulmonary tuberculosis with cavitation. He was promptly admitted to a sanatorium but died there in 1933. He was 20 years old and had been followed thirteen years.

In 1933 a boy of 9 reacted to tuberculin. He had been in a sanatorium from 1926 to 1933 for treatment of tuberculosis of the left hip, left wrist, left metatarso-phalangeal articulation and great toe. He was readmitted to the hospital in 1941 for arthrodesis of the left hip with bone graft from the tibia. There has since been no evidence of clinical disease. He is now 39 years old and has been observed thirty years.

When first examined in 1935 a boy of 10 was a reactor to tuberculin. His private orthopedist had diagnosed tuberculosis of the bones of the right ankle in 1934. He was treated surgically and has since been free from clinical disease. He is now 38 and has been followed twenty-eight years.

A boy of 13 reacted to tuberculin when first examined in 1926. He had pleurisy with effusion on the left side in 1924. In 1928 there was evidence of a perivertebral abscess at the level of the seventh, eighth, and ninth dorsal vertebrae. There was also marked destruction of the bodies of these three vertebrae and the intervertebral disks, which was determined to be tuberculosis. He entered a school for crippled children but was admitted to a sanatorium in 1937. On discharge in 1940 his disease was classified as arrested. The condition of his spine has remained unchanged and there has been no other evidence of clinical disease. He is now 50 years old and has been followed thirty-seven years.

A boy of 13 reacted to tuberculin when first examined in 1930. He had previously been treated for tuberculosis of the right hip joint. There was evidence of disease involving the upper lung field on each side. He was admitted

to a sanatorium and discharged in 1932. He has remained well. He is now 46 and has been followed thirty-three years.

A boy of 14 reacted to tuberculin when first examined in 1929. In 1922 he had been under treatment for tuberculosis of the right knee joint. No evidence of disease was found in either lung. He was admitted to a sanatorium in 1931 where surgery was performed. He was discharged in 1932. There has been no further evidence of clinical disease. He is now 49 years old and has been followed thirty-four years.

A boy of 14 reacted to tuberculin when first examined in 1921. He had tuberculosis of the left hip joint, but his lungs appeared clear. We did not see him again in our clinic and he died in 1924 of miliary tuberculosis. He was 17 years old with three years of follow-up.

A boy of 15 reacted to tuberculin when first examined in 1931. Kyphosis had developed due to tuberculosis following injury to the spine at the age of 1 year. Reexamination of the chest on three occasions in 1937 revealed no change. In 1941 he was apparently in good health and was working full time.

Of the 12 boys who had extrathoracic clinical tuberculosis 8 survived, 2 died and 2 have not been traced since 1941. The 8 survivors now range in age between 37 and 50 with a mean age of 44 years. They have been followed two hundred seventy person-years. One died from pulmonary tuberculosis at the age of 33, after thirteen years of follow-up. One died from tuberculous meningitis at the age of 17, after three years of follow-up. Two were well in 1941 after twenty-seven years of follow-up but they have not since been traced.

PULMONARY LESIONS IN GIRLS

In the group found to be tuberculin reactors between the ages of 6 and 12 there were 9 girls who had tuberculous pulmonary lesions before, or discovered at the time of, our first examination as follows:

There was only one child in this group who had a diagnosis of pulmonary tuberculosis before our first examination. A girl of 9, in June 1926, reacted to tuberculin. She had advanced bilateral cavitary pulmonary tuberculosis with acid-fast bacilli abundantly present in her sputum. Treatment was refused and she died August 12, 1926. History revealed that at age 4 she had empyema which was treated by aspiration. Eight months before we saw her a diagnosis of tuberculosis with acid-fast bacilli in her sputum had been made.

On first examination in 1931 a girl of 7 reacted to tuberculin. A small area of disease was demonstrated in the apex of the left lung. This appeared stable until 1933 when there was slight increase, and a small area of infiltration appeared in the apex of the right lung. The lesions continued slightly unstable through 1938 but definitely increased in 1939. By 1940 when she was 16 years old the disease was extensive in both lungs. Up to that time treatment had been refused. She was admitted to a sanatorium in June 1940 and died there in August. She was 16 years old and had been followed nine years.

In 1932 a girl of 7 reacted to tuberculin. She had a small infiltration in the apex of the left lung. She was admitted to a sanatorium but left against medical advice. She was readmitted five times, the last in June 1950, and died in August 1951 at the age of 26 with nineteen years of follow-up.

When a girl of 9 was first examined in 1931, areas of disease were found in the apex of each lung. These lesions responded well to treatment, so by 1934 only small residuals were in evidence. In 1936 the disease in the left lung and the upper lobe of the right lung was involved. She was then admitted to a sanatorium in July and discharged in May 1943. She has since had no evidence of reactivation or new lesions. She is now 41 years old and has been observed thirty-two years.

At the age of 9, in 1935, a girl reacted to tuberculin. A small area of disease was present in the upper lobe of the left lung. Periodic examination through 1939 revealed no change in appearance of the lesion. In 1940 extension was in evidence and another increase occurred in 1941 when acid-fast bacilli were found in her sputum. She was admitted to a sanatorium in 1940 and discharged in 1944. There has since been no evidence of progressive disease. She is now 37 years old and has been followed twenty-eight years.

In 1939 a girl of 9 reacted to tuberculin. Disease was demonstrated in the upper lobe of her right lung. She was admitted to a sanatorium in 1940. The same year tuberculosis was found in the right knee joint which was ankylosed surgically in 1943. She was discharged from the sanatorium in 1944. No other evidence of clinical disease has appeared. She is now 33 years old and has been followed twenty-four years.

A girl of 10, in 1932, reacted to tuberculin. There was evidence of infiltration and cavitation in the base of her right lung. She was admitted to a sanatorium and discharged in 1936 with apparent good recovery. She worked regularly but was again in the sanatorium from January 1948

to June 1949. She was admitted the third time in November 1949 and died in the institution in November 1950. She was 38 years old and had been followed eighteen years.

When a girl of 11 was first examined in 1926 she reacted to tuberculin. There was a small area of disease in the apex of the left lung. Slight increase was noted in 1928. She was in a sanatorium from July 1930 to December 1931 when the disease was classified as arrested. She was then married but was readmitted to the sanatorium in 1945 where she died a year later at the age of 31, after twenty years of follow-up.

A girl of 12 reacted to tuberculin when first examined in 1934. A small area of infiltration was present in the upper lobe of each lung. She was treated in a sanatorium from 1934 to 1939. She remained in good health until 1956 when she was again admitted to the sanatorium for a fifteen-month period of treatment. She has since remained well. She is now 41 years old and has been followed twenty-nine years.

Of these 9 girls, 5 died at ages 9, 16, 26, 28, and 31 years. They had sixty-five person-years of follow-up. The remaining 4 made good recoveries and are now 33, 37, 41, and 41 years old. They have had one hundred thirteen person-years of follow-up.

PULMONARY LESIONS IN BOYS

There were 6 boys who had pulmonary lesions discovered at the time of our first examination as follows:

A boy of 7, when first examined in 1926, reacted to tuberculin. Extensive disease was present in both lungs. He was readmitted in 1929 and discharged in 1931. In 1932 he died from chronic pulmonary tuberculosis and bronchopneumonia at the age of 13 with seven years of follow-up.

When first examined at the age of 9, in 1925, a boy reacted to tuberculin. He had evidence of advanced disease involving both lungs. He was promptly admitted to a sanatorium where he died three months later.

A boy was 11 years old when first examined in 1930. He reacted to tuberculin. There was evidence of disease in the upper lobe of his left lung. In 1932 this area appeared unchanged but a small area of disease had appeared in the upper lobe of the right lung. These 2 areas showed no demonstrable change through 1933. They gradually subsided and there has been no further evidence of clinical disease. He is now 44 years old and has been followed thirty-three years.

When a boy of 11 was examined in 1924 he reacted to tuberculin. Advanced disease was demonstrated in the upper lobe of his left lung. He was treated in a sanatorium until 1927. He was readmitted in 1928, and discharged in 1929. There has since been no evidence of clinical disease. He is now 50 years old and has been followed thirty-nine years.

In 1926 a boy of 12 reacted to tuberculin. There was a small area of infiltration in the apex of the right lung. He was in a sanatorium until 1927 when his disease was classified as arrested. In 1943 no change was found in his chest condition. There has since been no evidence of clinical disease. He is now 45 years old and is in good health. He has been observed thirty-three years.

On first examination at the age of 12, in 1925, this boy reacted to tuberculin. An area of disease was demonstrated in the upper lobe of the right lung. He was admitted to a sanatorium where he remained for three years. In 1928 there was definite increase in the area of disease and a lesion was demonstrated in the upper lobe of the left lung. He was promptly readmitted to the sanatorium and discharged in 1931 when the disease was classified as arrested. Since that time no clinical disease has been in evidence. He is now 50 years old and has been observed thirty-eight years.

Of the 6 boys, 2 died, 1 at 9, the other at 13. The 4 who survived are now 44, 45, 50, and 50 years old with one hundred forty-three person-years of follow-up.

DISCUSSION

Items presented in the first few pages of this paper such as, "only tuberculin reactors develop clinical disease," "administration of tuberculin tests by nurses," "primary tuberculous exceedingly benign," "clinical tuberculosis due to reinfections," "chronic forms of pulmonary tuberculosis usually result from long-standing infections," "diagnosis by roentgenographic shadows alone opposed," and "roentgenographic inspection of chests of all tuberculin reactors over 12 years imperative," are the result of extensive and intensive studies and observations so well documented over so many years as to leave no doubt as to their genuineness. Any tuberculosis program anywhere can be safely based on these well-established facts and practices.

The 46 cases presented had clinical tuberculosis (between the ages of 6 and 17) years before they were first examined by our staff. The most frequent attacks had been made on the skeletal system of 25 children. Only 6 died (2 pulmonary tuberculosis, 1 tuberculous meningitis, 2 cardiac conditions, and 1 glomerulonephritis). The early age when the skeletal system had originally been

clinically involved is impressive. The success of treatment with only 3 deaths from tuberculosis emphasizes the outstanding ability of orthopedic surgeons working before the antituberculosis drug era.

In the majority of the 9 girls and 6 boys of this series who had chronic pulmonary lesions when first examined, the lesions were small and did not cause significant external manifestations until later. From the treatment point of view this is the best time to start so as to prevent illness and communicability.

Follow-up on these cases emphasizes the importance of careful and prolonged observation after successful treatment of any given lesion. It must always be remembered that the clinical lesion is only one of many lesions in the individual's body and that one or more of them may later become clinical. For example, the girl in this series of cases who had successful nephrectomy at the age of 2 had pulmonary tuberculosis at 18.

A girl of 9 had tuberculosis of the left knee with successful treatment concluded when she was 12 years old. However, when she was 15 years old she had pulmonary tuberculosis which required five years in a sanatorium when she was 19 years old, and another period of hospitalization at the age of 26.

A boy at the age of 6 had his tuberculous right knee joint successfully treated. However, at the age of 19 he had advanced bilateral pulmonary tuberculosis from which he died at the age of 20.

Chronic pulmonary tuberculosis has never been reported as prevalent among grade school children. For example, in the Chadwick Clinics[12] which included examinations of 200,000 children in this age period only one case was found in each 3,300 examined. However, among the tuberculin reactors one case was found in each 700. Krause[13] estimated that in New York City one death from tuberculosis occurred among 800 tuberculin reactors. On the basis of these and other findings including those at Lymanhurst it has been recommended that in mass surveys and elsewhere x-ray films of chests of reactors be made only of those children 12 years and older. Although this is good practice economically it must be remembered that advanced chronic pulmonary tuberculosis does occur during this age period. In this series are a few examples. A girl of 9 who had advanced pulmonary tuberculosis in 1926 had had a diagnosis of advanced disease with acid-fast bacilli in her sputum eight months earlier. She died the same year.

A boy of 7 had advanced chronic pulmonary disease in 1926 from which he died at the age of 13. Another boy at the age of 9 had advanced chronic pulmonary tuberculosis when examined in 1925. He died the same year.

The possibility of the occasional tuberculin reactor child in the 6-12 age period developing communicable tuberculosis must be kept in mind.[14] They usually present symptoms which indicate complete examination. If they are not detected they can cause tuberculosis outbreaks in schools such as the one recently reported by Petter.[15]

Although the occasional tuberculin reactor between the ages of 6 and 11 develops clinical chronic pulmonary tuberculosis this form of the disease begins to appear more frequently at the age of 12 and increases as the years advance.[16] Thus, roentgenographic inspections of the chests of all tuberculin reactors beginning at 12 years of age should be made at least annually in order to find evolving lesions while they are minimal in extent and before they are disseminating tubercle bacilli.

ACKNOWLEDGEMENTS

The writer is deeply indebted to Dr. Gaylord W. Anderson, Director, School of Public Health, University of Minnesota, for providing ideal quarters and for encouragement in the conduct of our studies on tuberculosis. Special thanks are due Dr. Donald J. Cowling for his untiring and successful efforts in procuring additional funds to promote our studies.

Much credit is due Mrs. Marion Griffin, Mrs. Judith Brodie, Miss Cecile Hansing, and Miss Carole Stauff for their participation in assembling, tabulating, and analyzing data. Mrs. Alma Botkins is deserving of special credit for her strenuous and successful work in tracing former children and procuring necessary information about them. Her effort was greatly facilitated by Miss Helene Bender, Glen Lake Sanatorium.

The writer is grateful to many physicians in private practice for examining and providing up-to-date information concerning patients. Sanatorium medical directors, including R. W. Backus, T. E. Broadie, S. S. Cohen, J. B. Douglass, L. F. Flancher, V. K. Funk, L. S. Jordan, R. M. MacDonald, and M. M. Williams, have graciously compiled and transmitted data on patients treated in their institutions. Dr. D. S. Fleming, Director, Division of Disease Prevention and Control, and Miss Kathrine Gram, Minnesota Department of Health, and Dr. F. G. Gunlaugson, Director, Bureau of Preventable Diseases, Minneapolis, Minnesota, have provided much valuable information. Finally, extreme appreciation and thanks are due the former children, their relatives, and friends, who have cooperated so devotedly in providing the desired information.

Prepared with the aid of the H. Longstreet Taylor Tuberculosis Research Fund provided by the Minnesota Tuberculosis and Health Association, the J. Arthur Myers Research Fund of the University of Minnesota, and the Mrs. Ethel Noren Memorial Fund.

This paper was prepared for the H. D. Lees Series inasmuch as Dr. Lees was interested in tuberculosis for more than a decade while he practiced in North Dakota. Thereafter he was a member of the Lymanhurst Staff during the first decade of its existence and was familiar with many of the cases here reported.

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GRADUAL ONSET OF MILD PAIN in hip, thigh, knee, or back after minor stress and slight limp with moderate to severe limitation of rotation and abduction are characteristic of idiopathic avascular necrosis of the femoral head. This rare clinical entity is most common in middle-aged men and may develop in caisson workers and patients with sickle-cell anemia, congenital hemolytic anemia, Gaucher's disease, generalized arteriosclerosis, and lupus erythematosus. They may have a history of alcoholism or prolonged use of steroids. Roentgenographic features include a wedge-shaped area of increased radiopacity with the base at the superolateral weight-bearing aspect and the apex pointing into the head. A radiolucent band surrounds the wedge. The necrotic region may be seen as an atypical mottled area. Lateral views and planograms may be preferable. Essentially normal cartilage and definite necrotic, fibrous, and viable zones constitute major pathological findings. Avascular necrosis differs from osteoarthritis in that cysts and lipping are absent and the cartilage is intact, but osteoarthritis may complicate avascular necrosis and hinder diagnosis. Treatment by surgery gives the best results.

RICHARD J. PATTERSON, M.D., WILLIAM H. BICKEL, M.D., and DAVID C. DAHLIN, M.D., Mayo Clinic and Foundation, Rochester, Minn. J. Bone Jt. Surg. 46-A:267-282, 400, 1964.

FECAL LOSS OF CALCIUM, and usually of phosphorus, appears to be a characteristic of vitamin D—resistant rickets. Urinary excretion of calcium is decreased, and urinary excretion of phosphorus is either normal or decreased. Treatment with large doses of vitamin D or dihydrotachysterol (A.T. 10) reduces fecal excretion of calcium and phosphorus, probably because of increased absorption from the gastrointestinal tract. Metabolic balance studies in patients with vitamin D–resistant rickets were compared with those of controls matched for sex, age, and intake of calcium and phosphorus. Treatment of 9 patients with high doses of vitamin D or dihydrotachysterol resulted in mean increases in calcium and phosphorus absorption of 53 and 21%, respectively.

GUNNAR B. STICKLER, M.D., Mayo Clinic and Foundation, Rochester, Minn. J. Pediat. 63:942-948, 1963.

Winter Sports Injuries

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It seems wrong to discuss the bad side of a situation before giving credit to its good aspects. The exhilaration and challenge, as well as the body conditioning, of winter sports so far outweigh the occasional health hazards that one should like to discuss only these beneficial aspects. Nonetheless, we are here with a common purpose, and that is to discuss sports injuries. So I shall outline the injuries incident to the common winter sports and then discuss skiing injuries in more detail.

Winter sports in the United States are confined chiefly to the northern states paralleling the Canadian border, to the mountainous areas of the Rockies, and to the east and west coast mountain ranges. With no attempt to classify winter sports as to the age of the participants, or the technical difficulties of the sport, it may be said that the following winter sports are pursued by enthusiasts wherever climate will allow.

SNOWBALL THROWING

I am not being facetious in including this as a sport. While usually considered a childhood sport, throwing snowballs is sometimes indulged in by adults. It becomes a hazard if the hard snowball strikes the eye or ear. If a snowball is thrown at a passing motorist, he may lose control of his automobile.

SLIDING, SLEDDING, TOBOGGANING

Going down a hill on a sled is dangerous when the sled strikes or is struck by a passing car. Many deaths each year result from this unfortunate circumstance. Less serious injuries include broken teeth and facial lacerations from striking hard objeects, and fractures of the clavicle and forearm are not uncommon. Serious injury to the head may occur, and the viscera may be injured if the child is run over.

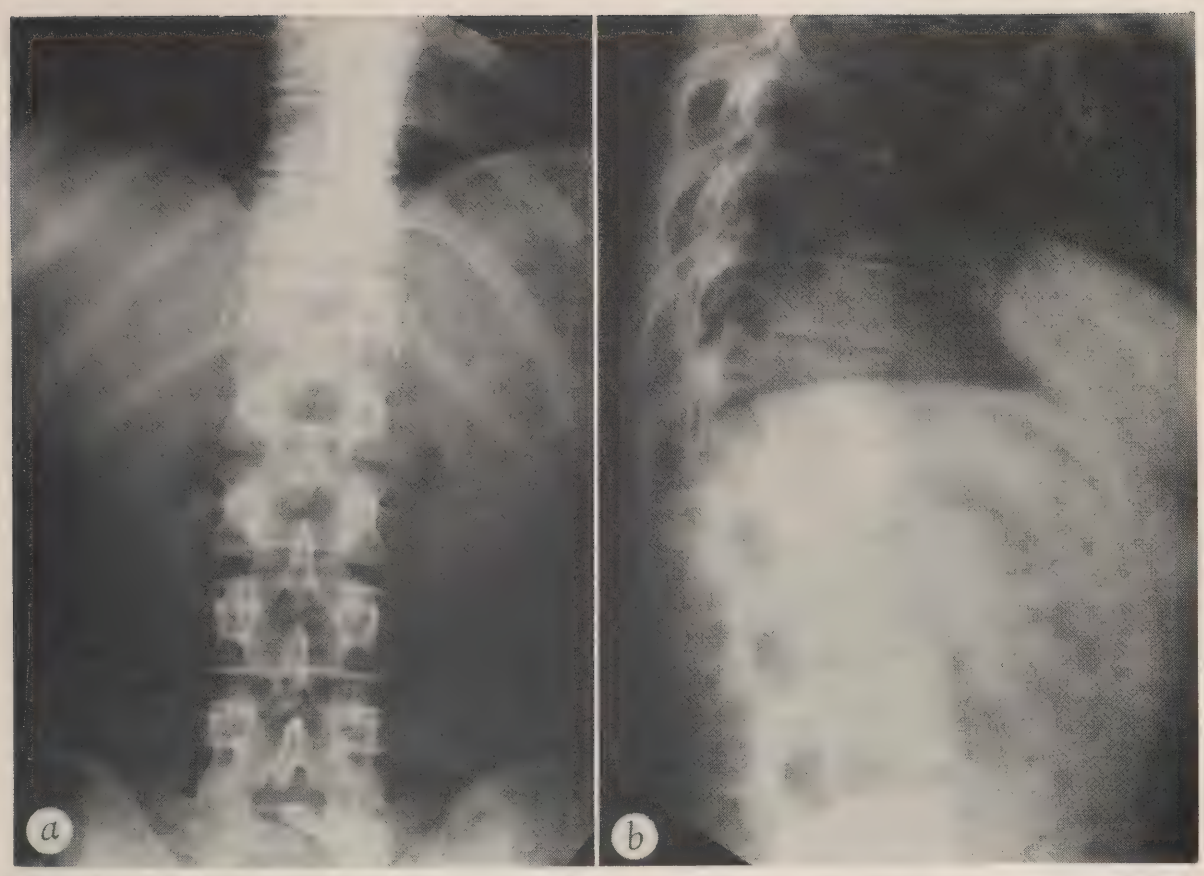
Tobogganing is one of our most hazardous sports per man-hour of participation. It is usually of 2 types. In the first and more common type, an open slope with reasonably heavy snow cover is found. From 1 to 8 people climb aboard and hold on, more or less, to ropes at the side of the toboggan. The person in front attempts to steer, and down the hill they go! This is a bit like playing Russian roulette, for a toboggan's direction can be controlled only slightly. The speed attained is sometimes considerable, and serious accidents may happen from this uncontrolled descent down a hill. A characteristic toboggan injury occurs when the toboggan goes over a bump, throwing the occupants high into the air. They come down in the same sitting position, more or less, and compression fractures of the spine often result (Figs. 1A and B). We see several such fractures each year in the community in which I live. A more serious problem occurs if the toboggan, after gaining considerable speed, strikes a stationary object such as a tree or a building. Damage to the cranium and its contents, and to the cervical spine, is not infrequent. In addition, the usual sprains and fractures of the extremities can occur, depending on circumstances. We should publicize the dangers of uncontrolled descent down a hill on a toboggan or sled so that the public is made aware of this hazard.

The second type of tobogganing involves a path or track for the toboggan, made either by icing snow or by building a wooden trough. In Quebec City, Canada, and in St. Paul, Minnesota, wooden toboggan chutes are constructed for the winter carnivals held there. These are many blocks long, and high speeds are attained. This is usually a safe form of tobogganing. The most common attendant injury is abrasion or laceration of the hands or knees as they scrape the sides of the chute.

CURLING

This sport is indulged in by very few in the United States. It had its origin in Scotland and is extremely popular in Canada. I have never seen a curling injury—only an occasional fall on the ice. Vigorous sweeping of the ice in front of the curling stone could result in sprain or

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Figs. 1A and B. Anteroposterior and lateral views of compression fracture of twelfth thoracic vertebral body caused by tobogganing

chronic strain to the wrist, shoulder, or back. And I have been told that finger injuries can result from crushing between the curling stones.

ICE SKATING

"Skater's nodule" is a peritendinitis, adventitious bursitis, and skin fibrosis of the leg at the upper edge of the skate boot. The anterior tibial tendon and common extensor tendons of the toes are involved in front and the tendo achillis posteriorly. Most skates today are properly padded with either sponge rubber or felt, and these lesions are less common than they formerly were.

Most injuries from skating occur from falls, and one sees the usual leg fractures and ankle sprains from this sport. Injuries from the blade of the skate, such as lacerations or puncture wounds, can occur.

ICE HOCKEY

My colleague, Dr. Joseph M. Janes,[1] has written on this subject. I have played ice hockey since I was able to walk and can say that the ice hockey injuries one sees today are not much different from those seen thirty-five years ago. While there is more body contact in the game today, the protective padding is such that these 2 factors tend to neutralize one another (Fig. 2). Headgear is now mandatory for our juvenile and school competitors and should decrease serious head injuries. Another major advance in padding is the use of the tendo achillis protective pad on the back of the skate. Lacerations and contusions to this tendon are now rare. The goal tender (guard) can lessen his chance of facial injuries by the use of a mask which, while still scoffed at by some, will gradually be used to a greater extent as the younger goalies become adjusted to it.

The injury in ice hockey may be from several sources:

1. The puck. This weighs about 6 oz. and can be shot at a speed of up to 80 mph.

2. The hockey stick. Injuries from the stick are usually in the form of lacerations, contusions, and fractures about the face and head. Injuries to the teeth are common.

3. The skates. Lacerations and puncture wounds may occur but do so less commonly than one might think.



Fig. 2. Hockey player with protective padding.

(From Janes, J. M.: Ice-Hockey Injuries. Clin. Orthopaedics. No. 23, 1962, pp. 67-74. By permission of the J. B. Lippincott Company.)

4. Intrinsic factors. Stress fractures, torn ligaments and tendons, and muscle rupture occur from undue effort on the part of the player.

5. Body contact. This produces most of the injuries in hockey, including ligament sprains, knee-cartilage injuries, muscle strains, contusions, fractures, and even ruptured viscera.

6. Injury of the player against the boards, the goal posts, or ice. These injuries may be quite serious and include cerebral concussion and injuries of the cervical spine.

7. Spectators. Foreign bodies thrown on the ice may cause a player to fall. In some of the more heated games a player may be struck by a spectator directly or by a thrown bottle or other object. Spectator and player enthusiasm occasionally reaches a very high pitch.

Actually, ice hockey injuries are not common, considering the extremely fast, aggressive, and competitive nature of the sport. One reason for this is the protective equipment used, as mentioned. Another is the absorption of the forces of gravity by the sliding of skates on ice.

The common injuries in ice hockey are, first of all, soft-tissue injuries. They include (1) lacerations about the face and tendo achillis, (2) muscle contusions, (3) sprains and strains, (4) arterial injuries that may occur at the wrist, groin, or along the leg and are caused by puncturing or laceration by the skate blades, broken sticks, or even the puck, (5) ruptured viscera, (6) cerebral injury, and (7) traumatic bursitis, which may (a) be prepatellar or olecranon or (b) appear in the form of a false bursa over the anterior tibial tendon or the tendo achillis (see Ice Skating).

Skeletal or bony injuries include (1) fractures of facial bones, clavicle, skull, spine, ribs, and bones of the leg or thigh and (2) acromioclavicular separation, which is perhaps the most common of all hockey injuries except those about the face. It usually results from striking the tip of the shoulder against the boards, the goal post, or another player. Sternoclavicular separation also may occur.

SKIING

Modern skiing began more than one hundred years ago in the Valley of Morgedahl, in the province of Telmark, Norway. The Austrians adapted the ski and developed the downhill or Arlberg technique; they shortened the ski and used a pole in each hand rather than the long



Fig. 3. Ski fracture of the fifth, fourth, and third metacarpals. Note spiral nature. Fracture of fifth metacarpal is distal to site of fracture of fourth metacarpal, rather than proximal to it as is usually the case.

single balancing pole originally used by the Norwegians. Controlled skiing was first introduced into the United States by Hans Schneider more than thirty years ago.

Skiing probably accounts for the majority of winter sports injuries. The tremendous interest in this sport, especially since World War II, has caused the ski slopes of America to be covered with eager, hopeful skiers of all degrees of skill. Many statistical studies have been made. Certain observations, as well as data on the numbers and types of injuries, have come from these studies. These include the necessity for physical conditioning before attempting downhill runs, the role of fatigue in injuries, and the effectiveness of ski bindings. Haddon and colleagues[2] found release bindings significantly effective in males but not in females. Beginners had more serious injuries than did experts. More injuries occurred in the afternoon than in the morning (fatigue). It is certainly true that surface conditions, including visibility, depth of snow, and iciness of the snow, contribute greatly to ski injuries. The type of ski boot, as well as how tightly it is bound to the foot, influences injury to a considerable extent.

The overall incidence of injury varies appreciably; studies by Ellison and colleagues[3] showed an incidence of 5.9 injuries per 1,000 man-days of skiing, but there are major variations as to age, sex, and skiing ability.

A typical ski injury consists of a sprained ankle and a sprained knee on the same side. The ankle sprain usually involves the anterior tibiofibular-fibulotalar complex rather than the anterior fibulotalar ligament only, as is seen in the common nonsports sprain. Ellison and colleagues found that 25% of all knee sprains were associated with either sprains or fractures of the ankle, as was found by Moritz[4] at Sun Valley as well. Fracture of the lateral malleolus is a so-called ski fracture; it accounted for 33.8% of the fractures and 12% of all injuries in the series of Ellison and colleagues. Fracture of both the tibial and fibular shafts was the second most frequent fracture, making up 21.9% of all fractures. It is usually at the junction of the middle and distal thirds of the leg, at the upper edge of the ski boot.

There is a trend in ski injuries toward more "boot-top" fractures as the boot gets higher and is more tightly laced and toward attritional rupture of the tendo achillis as the ages of skiers increase and stresses are put on collagen tissue that also is getting older and tears instead of stretches.

Skiing injuries are caused not only by falls but also by skiers' colliding with one another and by the apparatus of the ski lift. A skier may fall from the chair lift or may fall as the chair or T bar moves against him. A particularly dangerous type of lift injury is caused by the rope tow. Most ropes twist slowly as they move forward, and loose clothing can be caught in the twisting rope, preventing the skier from releasing at the top of the hill. If the automatic release fails to function as the skier strikes it, he can be carried into the pulley mechanism. Hanging may thus occur as the scarf becomes entangled in the rope, the automatic shutoff mechanism fails to work, and the skier is carried up into the pulley.

Acute pulmonary edema should be mentioned. This may occur at high altitudes in certain patients under the physical stress of skiing. It is treated by rest and the administration of oxygen.

I should like to close this discussion with an illustration of one of the first specific and classic sports injuries described. This is the ski fracture of the metacarpals.[5] In the series of Haddon and colleagues, metacarpal fractures accounted for only 1.3% of the total fractures seen. Allaria,[6] writing from Rome in 1950, stated that injuries to the hand represented 5.6% of all ski injuries. It does seem that this injury is more common in Europe than it is in this country. The first description of it was by Blauel[7] in 1909. Logroscino,[8] in 1937, confirmed this as an injury specific to skiing and better defined the mode of injury. The skier falls forward onto his clenched hand, which is grasping the grip of the ski pole. The surface is usually hard-packed or icy snow. The force of the fall is on the ulnar surface of the hand, and, as the skier falls forward and rolls his body onto the hand, a torsional force is applied and the metacarpals are fractured from ulnar to radial and from proximal to distal in a classic spiral fashion (Fig. 3). Any or all of the lateral 4 metacarpals may be involved. What makes this typical of ski injury is the spiral nature of the fracture and the involvement from proximal to distal as one goes from the ulnar to the radial metacarpals. Boxing produces a somewhat similar fracture which, however, tends to be less spiral and seldom involves more than one metacarpal. Knuckle injuries at the distal neck of the metacarpals occur in many sports from striking heavy objects, and these, too, are not usually spiral but transverse.

Generally, these fractures are in good position and require only a dorsal plaster of paris splint until the callus consolidates. If more than a centimeter of shortening is present, however,

they should be manipulated or opened and fixed with Kirschner wires or with traction.

This historic fracture should be remembered for its close association with sports, and even though rather rare it is classic when seen incident to skiing.

Read at the meeting of the Texas Society of Athletic Team Physicians, Houston, Texas, April 23, 1964.

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PROGNOSIS FOR ANEURYSM of the thoracic aorta is best when the defect is small or caused by trauma. Survival is affected adversely by a large aneurysm, an age of 50 years or more at the time of diagnosis, and associated diastolic hypertension or other cardiovascular diseases. Pain, dyspnea, dysphagia, dry cough, hoarseness, and murmurs usually indicate the patient has a large lesion with poor prognosis. Five- and ten-year survival rates are significantly lower for patients with an aneurysm than for persons of the same age and sex distribution in the general population. Fusiform aneurysms are most common and are most often found in the descending thoracic aorta. Saccular aneurysms are usually located in the ascending aorta. These conclusions are based on study of 107 patients with aneurysms that were not treated surgically.

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Circulation 29:176-181, 1964.

HEMIGASTRECTOMY AND VAGOTOMY is recommended treatment of duodenal ulcers in children. Under medical therapy, ulcers persist or recur in half the cases. No recurrence follows operation, and growth or development of the child is not affected. Symptoms include chronic duodenal obstruction with vomiting, intractable pain, recurrent melena, and hematemesis. The ulcer frequently is demonstrable roentgenographically. Five gastroenterostomies and 5 gastric resections were done in 10 patients less than 16 years old, with no operative deaths. A 75% Billroth II-posterior Pólya-Hofmeister procedure was done in 2 patients and a 50% hemigastrectomy and bilateral abdominal vagotomy in 3.

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Postgrad. Med. 35:175-179, 1964.

Management of Spontaneous Splenic Rupture in AHG Deficient Hemophilia

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THE MEDICAL MANAGEMENT of hemorrhagic problems in patients with classic hemophilia has steadily improved. Increased awareness of bleeding disorders on the part of physicians, more accurate laboratory diagnostic techniques, and significant advances in the therapeutic armamentarium have contributed to the improvement in prognosis.[1]

Because surgical procedures in hemophiliacs have been attended by a high morbidity and mortality, a program of careful preoperative and postoperative management has been essential in the care of these gravely afflicted patients.

The patient to be reported was severely deficient in antihemophiliac globulin (AHG, factor VIII) and required splenectomy after spontaneous rupture of his spleen. His course was relatively uncomplicated, and the fear of severe hemorrhage following the massive abdominal surgery did not materialize. This experience prompted summarization of current techniques for the control of hemorrhage during surgical intervention in hemophiliacs.

CASE REPORT

An 11½-year-old boy with classic hemophilia (Fig. 1) was admitted to the University of Minnesota Hospitals for the fifteenth time on Jan. 22, 1964. Previous admissions had been for treatment of soft tissue hematomas, hemarthroses, lacerations, deciduous teeth extractions, and 1 episode of hematemesis associated with gastroenteritis. Laboratory documentation of his hemophilia had included a Lee-White clotting time of one hundred twenty minutes, partial thromboplastin time greater than four hundred seconds, and AHG activity level of less than 1% on specific assay. The family history revealed that 3 maternal great uncles were "bleeders."

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Asymptomatic splenomegaly was first noted on Dec. 1, 1958, and again on a routine physical examination on Jan. 1, 1964. On Jan. 3, 1964, he was admitted to the hospital because of left lower quadrant pain and vomiting. He responded to symptomatic care at that time. On Jan. 8, 1964 he complained of left upper quadrant "rumbling pain." An enlarged spleen 3 cm. below the left costal margin was again noted. On Jan. 22, 1964, the boy complained of pain in the left upper abdomen and vomited undigested food 4 times. He became pale and weak, and immediately developed signs and symptoms of shock. Left upper quadrant tenderness and fullness were noted. A mass extending 9 cm. below the left costal margin was palpated. A diagnosis of spontaneous subcapsular splenic hemorrhage was entertained. Immediate measures were instituted to correct the state of shock. He responded rapidly to infusions of fresh frozen plasma and fresh whole blood.

The patient did well on a planned regimen of treatment with plasma and AHG rich fibrinogen. His abdominal mass became smaller and was no longer tender. The transfusion therapy was stopped after the eighth hospital day and the patient continued to be asymptomatic. Platelet count rose to one million on the twelfth hospital day.

On the thirteenth hospital day, while still on strict bed rest, the patient woke with mild upper respiratory symptoms, including a cough. Later that morning he complained of left upper quadrant cramping and vomited. Shortly afterward the patient went into shock. Transfusion with fresh plasma and whole blood was immediately started.

Recurrence of subcapsular splenic hemorrhage was evident. Further purely conservative measures were deemed inadequate since minor trauma had prompted the recurrence of hemorrhage. Preparation for abdominal surgical exploration were begun. During the eighteen hours prior to surgery he received 420 cc. of fresh whole blood, 525 cc. of fresh frozen plasma, 175 cc. of packed red blood cells, and 6 gm. of fibrinogen A.H.F. The patient was in satisfactory physical and hematological condition when he was taken to the operating room. Vital signs were normal, hemoglobin was 12 gm. percent, and P.T.T. was one hundred twenty seconds. Splenectomy was accomplished with surprisingly little hemorrhage. Blood loss was estimated to be 500 cc. A large "football" size localized hematoma was found in the left upper quadrant of the abdomen. Careful dissection of the hematoma away from contiguous

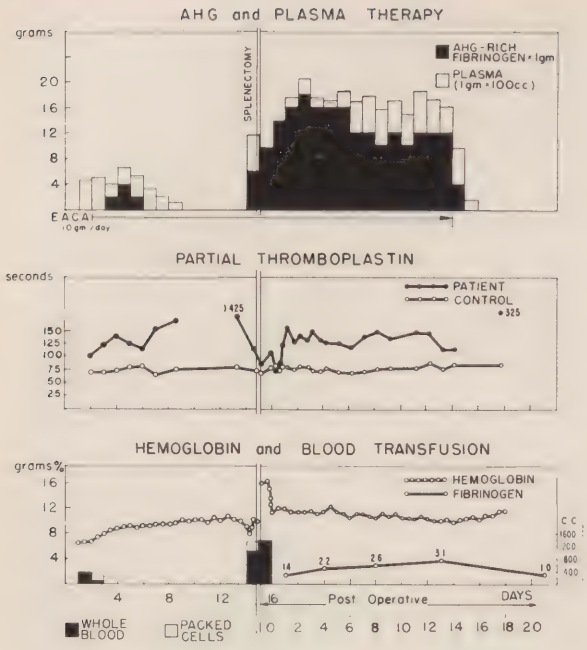


Fig. 1. Clinical course of patient's progress before and after splenectomy. Patient's bleeding diathesis controlled by use of partial thromboplastin time

structures revealed it to be associated with a large, somewhat necrotic, splenic mass. The spleen was carefully mobilized with meticulous attention paid to control of bleeding. The major vessels were clamped and ligated, and the spleen was removed together with the hematoma. A large rent was found on the posterior surface of the spleen (Fig. 2). The operative site and entire abdomen were carefully examined for evidence of persistent bleeding. After complete control of hemostasis, the abdominal incision was closed layer by layer. The patient tolerated this procedure very well. He received 2,000 cc. of fresh whole blood during the operation.

The immediate postoperative course was stable, and therapy consisted mainly of infusions of Fraction I preparations with intermittent transfusions of fresh frozen plasma. The postoperative course continued to be very stable and his incision healed rapidly; at no time did skin ecchymoses appear at the operative site.

On the seventh postoperative day 1+ albuminuria was noted. This persisted for approximately three weeks. Also, the patient was found to have markedly elevated plasma fibrinogen levels which were apparently well tolerated. On the tenth through the fourteenth postoperative days alternating sutures were removed without evidence of hemorrhage. The wound was well healed. On the fifthteenth postoperative day Factor VIII replacement therapy was abruptly discontinued without consequence. By the eighthteenth postoperative day the patient was ambulatory, taking regular diet, and suffering no ill effects. He was discharged on his twenty-first hospital day.

After two asymptomatic months at home the patient suddenly developed a massive hemothorax. This was treated with plasma, AHG fibrinogen, and whole blood for the first twenty-four hours, and then aspiration of the hemothorax by thoracentesis. Because of increasing hemothorax and dyspnea even with oxygen, and because the apex of the heart was deviated to the right midclavicular line, thoracotomy and removal of all blood clots was accomplished. The postoperative course was as before except for the development of refractoriness to plasma therapy. The latter was attributed to a circulating anticoagulant and all plasma therapy was discontinued. Gradually his hemothorax has cleared and there has been a loss of his circulating anticoagulant (Table 1 and Figs. 3 and 4).

DISCUSSION

Hemarthroses, hematomas of subcutaneous tissue, hemothorax, and severe intraabdominal bleeding have all been noted to resolve easily and readily with plasma therapy.[2] In complications of hemophilia that require surgery, careful operative technique with meticulous attention to hemostasis is mandatory. The removal of an entire organ by careful suture ligation represents a more favorable situation for control than one in which diffuse bleeding is present in a tissue, or where extensive inflammation or adhesions are present.

Plasma Factor VIII activity levels of 5% to 10% normal are adequate to provide hemostasis for minimal injury in the hemophiliac.[3,4] In cases of severe hemorrhage, or surgical intervention, levels of 30% or more are required.

In the maintenance of effective Factor VIII activity, several factors must be taken into consideration. First, the half life of AHG in vivo is four to seventeen hours.[5,6,7] This necessitates frequent infusions. Second, the presence of infection or tissue necrosis will increase the rate of utilization of Factor VIII. Third, there is a variation in the activity of Factor VIII in the infused plasma. Fourth, the severity of deficiency in AHG in the individual patient will affect the

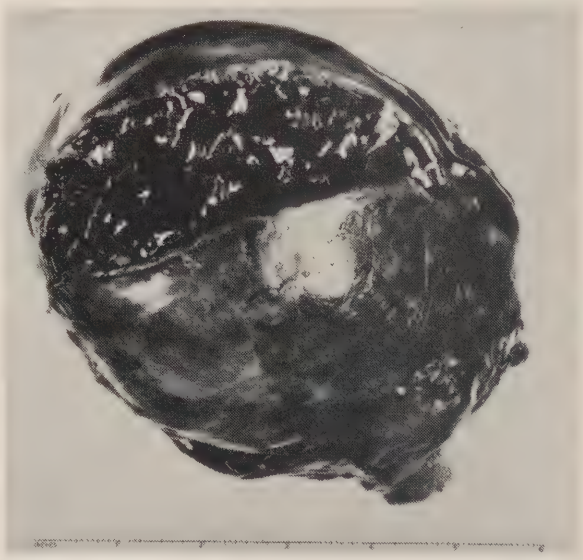


Fig. 2. Bleeding from spontaneous rupture of spleen caused original problem.

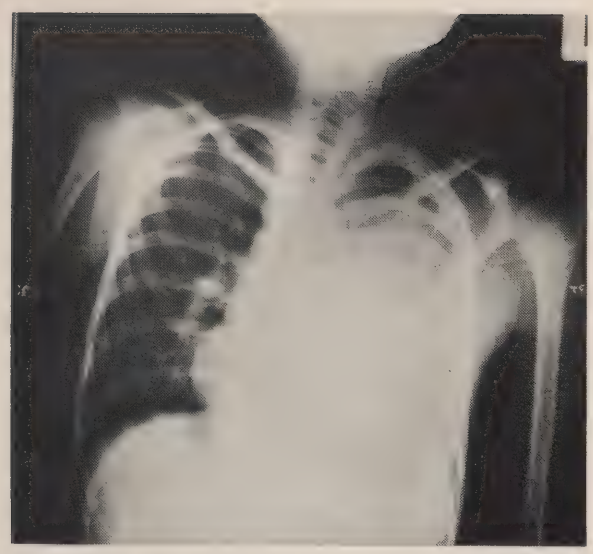


Fig. 3. Hemothorax that developed two months post-splenectomy

volume of plasma required for adequate Factor VIII activity.

During the past ten years the use of plasma Fraction I of Cohn has been employed with increasing success.[8,9,10] This was the major agent used in our case. This product has its greatest advantage by virtue of the higher concentration of plasma Factor VIII activity by volume that can be obtained. Only 1 gm. of fibrinogen A.H.F. dissolved in 30 cc. need be infused to achieve the same Factor VIII activity provided by 100 cc. of fresh plasma. The use of fresh whole blood or fresh plasma therapy is restricted by the volume that can be infused. The use of lyophilized Fraction I of Cohn alleviates this problem. Moreover, this product is indefinitely stable when stored properly.

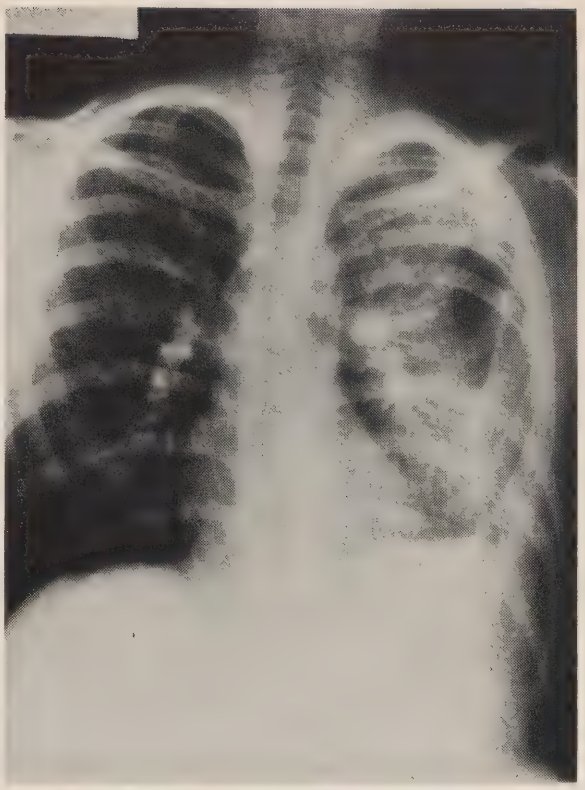


Fig. 4. Resolution of hemothorax occurred after surgical drainage in four-week period.

The need is imperative to adopt a single coagulation test which will be both sensitive and easily done for following level of AHG infused.[11,12] For this the most clinically useful method is the partial thromboplastin time (P.T.T.).[13–17] In this patient, levels between one hundred twenty and one hundred forty seconds were indicative of adequate hemostasis.

Maintenance of an adequate level of Factor

TABLE

THROMBOPLASTIN GENERATION TIME

		1′	*2′*	*3′*	*4′*	*5′*	*6′*
Control	Normal serum 1:10 dilution Normal $BaSO_4Pl$ 1:5 dilution Normal platelets + 0.2 cc. saline	>60″	33.8″	14.2″	14.6″	13.6″	13.7″
	Normal serum 1:10 dilution Normal $BaSO_4Pl$ 1:5 dilution Normal platelets + 0.2 cc. Wilson $BaSO_4Pl$ undiluted	50.6″	38.8″	——	52.8″	33.0″	21.8″
Incubated two hours at 37° C.	Normal serum 1:10 dilution Normal platelets Normal $BaSO_4P$ 1:5 Wilson $BaSO_4Pl$ undiluted	>60″	>60″	>60″	>60″	40.8″	40.0″

VIII was achieved by a planned program of infusion. Adequacy of hemostasis was determined by cessation of hemorrhagic signs, maintenance of hemoglobin, and persistent shortening of the patients prolonged partial thromboplastin time. The volume of infusion sufficient to achieve these goals of hemostasis, based on the experience of ours and others, was 15 cc. per kilogram of body weight of fresh frozen plasma, or its equivalent, in the first twelve-hour period, and 10 cc. per kilogram of body weight of fresh frozen plasma, or its equivalent, in each subsequent twelve-hour period. The problem of hypervolemia was circumvented by utilizing fibrinogen A.H.F. for the major amount of Factor VIII administered. Whole blood was not required after initial restoration of hemoglobin during the first twelve hours of treatment.

One major complication of intensive plasma therapy is the development of resistance to plasma. Because this may be acquired rapidly and because additional plasma only increases the resistance, early detection is mandatory. The daily use of P.T.T. provides a safeguard. A lack of maintenance of stated levels, as described by a rising P.T.T. time despite adequate plasma infusions, indicates such a resistance. Whether or not this may be due to infectious necrosis or a circulating anticoagulant may then be tested and appropriate countermeasures undertaken.

E-ACA (epsilon amino caproic acid) was used in this patient as part of a general study of the effect of E-ACA in hemophilia. Previous reports from this center have indicated that hematuria occurring in hemophiliacs could be controlled by administration of E-ACA.[18]

E-ACA has also been studied by ourselves and by others as primary therapy of hemophiliac complications.[19] In a double-blind control study we had observed no superiority of E-ACA to placebo. E-ACA has also been used in 2 other patients who have undergone major surgery.

The rationale for this therapy was both to provide inhibition of lysis of any fibrin formation and to prevent Factor VIII destruction. This would then weight the hemostatic equilibrium toward clot maintenance. Excess fibrinolysin activity was not the rationale for the use of E-ACA as in postoperative heart surgery reports from this center.[20] Newcomb,[21] however, in noticing increasing consumption of Factor VIII on the sixth to eighth postoperative day in his patients postulated a mechanism such as increased fibrinolysis. The place of E-ACA as adjunct in therapy of hemophilia must await further study and analysis.

Spontaneous rupture of spleen and splenectomy in hemophilia[22–24] has been consistent with increasing use of surgery in these patients as reported in the literature.[25–35] Surgical therapeutic intervention must be tempered by knowledge that in reporting cases in literature overt failures and demise will not be as readily reported as the successes. Despite our increasing knowledge and relative stability of our patient's course, surgical therapy must be held as an appropriate last resort in hemophilia.

SUMMARY

1. A case of spontaneous splenic rupture in a classical hemophiliac patient is presented.

2. After conservative management was unsuccessful, splenectomy was accomplished with surprising ease.

3. The medical and surgical principles for successful management are discussed.

Supported by grants from the University of Minnesota Graduate School, Cardiovascular Clinical Research Program Project, USPHS No. HE-05341-05 and USPHS AM-02917-05.

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ATOPIC DERMATITIS persists for an average of twenty-seven years in mild and thirty-two years in severe cases. About two-thirds of the patients have a family history of atopy, and more than half are prone to asthma, hayfever, urticaria, migraine headache, or rhinitis. Hyposensitization therapy is of little value, and eosinophil counts are inaccurate predictors of dermatitis severity or course. However, a temperate or dry climate, relaxation, relief of tension, oral and topical steroids, and avoidance of primary irritation promote relief of symptoms. Review of records of 492 patients with atopic dermatitis showed an average age of 20 years on first examination at the Mayo Clinic, but a median age of 4 months at onset of eczema. Twenty years after diagnosis, only 40% with mild and 29% with severe atopic dermatitis were free of lesions, based on a 45% follow-up questionnaire return.

HARRY L. ROTH, M.D., and ROBERT R. KIERLAND, M.D., Mayo Clinic and Foundation, Rochester, Minn. Arch. Derm. 89:209-214, 1964.

MORTALITY RATE IS DECREASING in total open-heart surgery, primarily because of improved judgment and technique. In 744 operations during 1957-63, the 32% mortality rate early in the period was reduced to 4%. Operative deaths most often were related to such problems as incomplete repair of septal defect, only partial relief of pulmonary stenosis, inappropriate methods of valve repair, surgically induced heart block, air, or calcium embolism, and infection.

DWIGHT C. MC GOON, M.D., THOMAS H. ALLEN, M.D., and EMERSON A. MOFFIT, M.D., Mayo Clinic and Foundation, Rochester, Minn. Arch. Surg. 88:681-688, 1964.

Tracheostomy

A Reappraisal

THEODORE J. SCHARF, M.D., and DANIEL E. SMITH, M.D.

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TRACHEOSTOMY, a centuries-old surgical procedure, was considered only as an emergency lifesaving measure, until little over a decade ago. Pulmonary aeration via tracheostomy is most commonly employed in cases of glottic obstruction due to foreign body or infection; in head, neck, and thoracic trauma; and in neurological dysfunction and incident to various surgical procedures. In recent years, the observation that the indications for tracheostomy have been expanded[1,2] to include an ever-increasing number of patients with primary pulmonary disease has prompted the evaluation of 80 consecutive procedures performed for patients 55 to 78 years of age with chronic pulmonary disease at the veterans hospital, Albuquerque, New Mexico, in the past three years. The period of follow-up lasted until the tracheostomy tube was removed or until the patient died with the tracheostomy in place.

The value of tracheostomy seems obvious, but it is also evident that indications are often overextended, complications do occur, and the ultimate death rate is high. Also, performance of a tracheostomy is often delayed beyond the point where its benefit to the patient dying from respiratory failure can reasonably hope to be successful. Too often, tracheostomies are done on terminal patients in a heroic but futile last effort. An appraisal of these observations has brought out many features which deserve emphasis.

Indications. Basically, tracheostomy is indicated in the management of correcting an underlying pathological process impairing the respiratory function. Intermingled with the use of tracheostomy as a temporizing procedure, that is, buying time for the patient while ventilatory homeostasis is being restored, a new concept is emerging: the permanent tracheostomy necessary to sustain life in chronic pulmonary cripples. In this series, the predominant indication was for nonsurgical pulmonary disease.

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Table 1 lists the indications and deaths. None of the deaths was attributable to tracheostomy itself. The mortality rate in those patients with nonsurgical pulmonary disease is disturbing, but equally disconcerting is the abbreviated length of survival from time of tracheostomy (Tables 2 and 3).

Survival time. From tables 2 and 3, it is apparent that the critical period is within the first twenty-four to forty-eight hours following tracheostomy. This probably reflects a summation of effects which, in retrospect, may have led to a different series of events. Of the 16 deaths which occurred within twenty-four hours, a review of the records revealed it was apparent 9 should have had tracheostomy at least two to four days earlier. All these patients initially had been managed with transnasal endotracheal aspiration, intermittent positive pressure breathing (IPPB), and antibiotics. When it is evident the patient is not making marked early improvement by these measures, tracheostomy should be done. The morphological appearance of lungs in patients dead from chronic bronchitis (Fig. 1) suggests that earlier vigorous treatment including tracheostomy may have been lifesaving. When patients have passed over the brink of pulmonary reserve, few will be retrieved by tracheostomy. However, at autopsy, 5 patients with tracheostomies revealed excessive bronchial secretions and plugs reflecting inadequate endobronchial aspiration. This only serves to reemphasize the fact that tracheal fenestration without intensive aftercare represents a useless operation (Fig. 2).

Transnasal endotracheal aspiration will usually clear secretions to the carina. This type of aspiration is inadequate in patients with an ineffective cough or who are exhausted from the effort to respire because they are unable to raise mucus from below in order that it may be removed. The course in these patients is one of relentless respiratory failure for which tracheostomy will be of little or no benefit late in the course of their illness. While, theoretically, bronchial aspiration through a tracheostomy tube

TABLE 1

INDICATIONS AND DEATHS

Indication	*Number of patients*	*Deaths*
Emphysema	11	4
Pneumonia	34	20
Trauma	6	1
Neurological	6	6
Elective (surgical)	20	13
Retained secretions and dyspnea	9	6
Total	80	50

62% mortality for all indications

56% mortality for nonsurgical pulmonary disease

TABLE 2

LENGTH OF SURVIVAL FROM TIME OF TRACHEOSTOMY

Days	*Deaths*
0-1	16
2	6
3	2
4	2
5	3
6	3
7	2
8	
9	2
10	1
11	2
14	1
16	1
22	1
1-2 mos.	3
2-6 mos.	5
Total	50

TABLE 3

SURVIVAL FROM TIME OF TRACHEOSTOMY FOR PULMONARY INSUFFICIENCY

Days	*Deaths*
0-1	6
2	7
3	2
4	2
5	1
6	1
7	1
8	
9	2
10	1
11	1
Total	24

54% dead within forty-eight hours

is more efficient and the catheter tip can reach the lower bronchial tree with more assurance, it is equally obvious that if the method of catheter aspiration is not performed assiduously, there will be little effect on the ultimate outcome.

Other causes of death undiagnosed before autopsy and unrelated to pulmonary insufficiency were perforated duodenal ulcer, 1; gastrointestinal hemorrhage, 3; myocardial infarction, 3; pulmonary embolus, 2; subdural hematoma, 1; and peritonitis, 2. In all these patients, known preexisting pulmonary disease led the physician from the true premortem diagnosis and into a tracheostomy for supposed primary respiratory failure.

Complications. The complications are enumerated in table 4. Bleeding was the most frequent complication. Blood which trickles into the bronchial tree has the serious detrimental effect of nullifying the advantages of the tracheostomy. In this series, bleeding was of minor consequence and required only packing for control. The 2 wound infections were not serious. In one patient who developed a pneumothorax, prompt recognition that he suddenly became worse and a tube thoracotomy were lifesaving. Interestingly, all the patients with complications are survivors.

TABLE 4

COMPLICATIONS

Bleeding	5
Wound infection	2
Poor fit	2
Pneumothorax	1
Pain	2
Failure to close	1
Total	13

TABLE 5

BACTERIOLOGY (25 PATIENTS)

	Cultures
Staphylococcus aureus	22
Streptococcus	12
Pneumococcus	4
Pseudomonas	5
Neisseria	3
Aerobacter	2
Total	48

Bacteria from tracheal aspiration. Twenty-five patients had bacteriologic studies. Six different organisms were obtained in 48 cultures (Table 5). Staphylococcus aureus was the worst offender. Also noteworthy are 5 cultures of Pseudomonas from a single pulmonary disease ward.

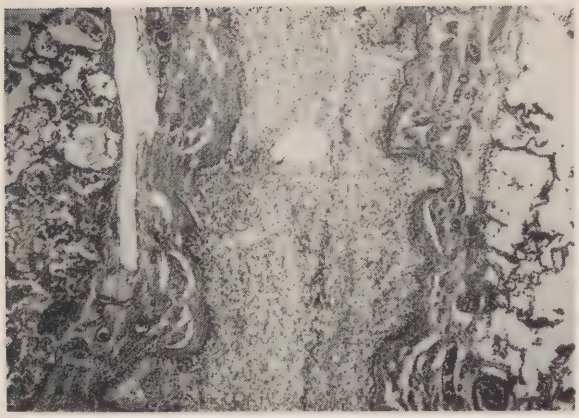


Fig. 1. Photomicrograph revealing mucopurulent plug in medium-size bronchus



Fig. 2. Left lung of patient who had fatal chronic bronchitis. Retained mucopurulence seen in lower bronchi. Tracheostomy performed forty-eight hours before death

All the patients having cultures were on antibiotics, usually penicillin, streptomycin, or tetracycline. In certain cases where staphylococci predominate, the use of sodium methicillin (Staphcillin) or sodium oxacillin (Prostaphlin) should be considered, since the exuberant mucopurulent secretions establish a favorable culture medium for overgrowth and resistant strains.

Planning and care of the tracheostomy. Because of the remarkable mortality rate in patients with tracheostomy, we no longer subscribe to its performance when it is an unconscious suggestion or when we "think of it." Rather, with deliberate haste, the events leading up to consideration of tracheostomy and a value judgment of the patient's likelihood for signficant survival time with or without the tracheostomy are weighed. By this comprehensive approach, it is hoped that a more intelligent use of tracheostomy will result, especially reflected in longer survival times.

Once a tracheostomy is elected, the patient is moved to the operating rooms where good lighting, adequate assistance, and anesthesia are available. Bedside tracheostomies are decried, representing the antithesis of the planned procedure in the operating room. The hazards of bleeding, inadequate suction, poor lighting, insufficient assistance, and infection are setups for an unfavorable outcome.

The care of the tracheostomy must be controlled and preferably is done by the physician. Diligence regarding sterile technique is the sine qua non of management. With ablation of the cough reflex after tracheostomy, secretions can only be effectively removed by judicious, frequent, and attentive aspiration in both bronchial trees. Humidification of the air entering the tracheal stoma is important in order to keep the secretions moist and liquid. A plastic humidor which "caps" the tracheostomy is connected by a long, crimped plastic tubing to wall oxygen. The oxygen passes through an aerosol mixture resulting in a saturated vapor. The inner cannula of the Jackson tube should be cleaned after each suctioning to prevent crust formation. We have had limited experience with the Kistner tube[4,5] but have found it to be of merit as a permanent tracheostomy (Fig. 3). Patient satisfaction has been fa-



Fig. 3. Kistner tracheostomy tube in patient with severe emphysema. The ill-fitting tube (above) replaced with properly seated tube (below).

vorable, since they are able to converse without mechanically occluding the tracheal stoma.

SUMMARY AND CONCLUSIONS

1. Tracheostomy procedures have been reviewed over a three-year period. The mortality rate in patients with tracheostomy for all indications is 62%.

2. Indications for the procedure reveal that 56% were for nonsurgical pulmonary disease. Tracheostomy for compromised pulmonary insufficiency should be done earlier in the disease, not as a terminal event. A 54% death rate under forty-eight hours infers that performance was injudicious or inordinately delayed.

3. Despite the extended indications for tracheostomy, it should not be regarded too lightly or performed hastily, since definite complications can occur, and the ultimate mortality is high.

4. Diligence in tracheostomy aftercare is emphasized, since some early deaths were attributable to inadequate bronchial aspiration.

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IN ENCAPSULATED SUBDURAL HEMATOMA in patients past infancy, simple trephination with evacuation through burr holes gives better results than craniotomy with membranectomy. Bilateral hematomas must be ruled out by preoperative studies or at operation. Openings are made in the midtemporal and posterior parietal areas and in front of the coronal suture, if necessary. The dura mater and outer membrane are opened, margins coagulated, and the intermembranous space irrigated thoroughly with warm saline or Ringer's solution. A Penrose drain is introduced, with removal in twenty-four to thirty-six hours. The patient is maintained in a 30° Trendelenburg position for three to five days. Hydration is necessary. Of 69 patients with encapsulated subdural hematoma, both immediate and long-term results were better in 50 who received initial clot evacuation through burr holes than in 19 with craniotomy and removal of membrane.

HENDRIK J. SVIEN, M.D., and JOSEPH E. GELETY, M.D., Mayo Clinic and Foundation, Rochester, Minn. J. Neurosurg. 21:172-177, 1964.

HEAVY INSECT SPRAY EXPOSURE may cause acute myelogenous leukemia. At least 100 cases of familial leukemia have been recorded, and several nonfamilial cases have occurred after exposure to hydrocarbons and their derivatives when patients probably were genetically susceptible. Acute myelogenous leukemia developed in a mother and son after heavy exposure to elm spray blown through an open window. Leukemia also was caused by toxic exposure in 2 cousins eight months after exposure to hexachlorocyclohexane insecticide.

KARL H. KOLMEIER, M.D., and EDWIN D. BAYRD, M.D., Mayo Clinic and Foundation, Rochester, Minn. Proc. Mayo Clin. 38:523-531, 1963.

Ethchlorvynol Intoxication and Severe Abstinence Reaction

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Fargo

The use of tranquilizing drugs has been established in our medical therapy. In the past ten years this group of drugs has become one of the most widely prescribed and administered group of medicines in the pharmacopoeia. In response to the many articles on the beneficial effects of these drugs, articles on side effects, toxicity, habituation, and addiction have been published.[1–8] No previous report on abstinence reactions following ethchlorvynol has been reported. The case presented here illustrates a situation in which the patient, without the physician's knowledge, took an excessive dose of ethchlorvynol and developed neurological manifestations of drug toxicity. Upon discontinuing the drug the patient experienced a severe abstinence reaction. Haizlip and Ewing[7] classified abstinence reactions as being mild if the only symptom was insomnia and muscle twitching, moderate if the patient showed severe insomnia and a psychotic episode clearing within thirty-six hours, and severe if the patient had a seizure or a prolonged psychotic episode.

CASE REPORT

The patient was a 20-year-old female who was first seen on Dec. 30, 1957, because of nervousness, apprehension, and a sensation of shortness of breath. She dated the onset of these symptoms to November 1957, when she had discomfort in a small, warm room under conditions of tension. The past history revealed no operations or previous illnesses. Her father died in an accident and there were no familial diseases. The patient was married and had 4 children. Review of systems was normal except for shortness of breath and a sensation of pounding of her heart during spells of nervousness. Physical examination revealed a well developed, slender Caucasian, 5′ 2″ in height and weighing 109 lb. Her blood pressure was 120/80, pulse 102, and temperature 98.6° F. Her hands were cold, and there was a 2+ tremor not increased by motion. The rest of the physical examination was completely normal. Laboratory examination disclosed a hemoglobin of 13.5 gm. percent, a red cell count of 4.2 million per cc., and a white cell count of 6,450 with a normal differential. The sedimentation rate was 5 according to the uncorrected Wintrobe method. The urinalysis was normal. The protein-bound iodine was 5 μg. percent, and the twenty-four-hour I^{131} uptake was 36%. The chest X-ray was normal. The diagnosis was acute anxiety neurosis with hyperventilation syndrome. Hyperventilation for two minutes reproduced the patient's symptoms and her pulse rose to 120. The patient was treated with reassurance and given suggestions for release of tension and prochlorperazine as the dimaleate, 15 mg. twice daily. The patient improved on the above program and was seen on Feb. 4, 1958, and March 17, 1958. Her medication was then discontinued. On April 14, 1958, the patient was seen again with a recurrence of symptoms. At this time she was having trouble sleeping, in addition to her symptoms of shortness of breath and nervousness. The physical examination was unchanged except that her weight was down to 104 lb. Her medication was restarted and the anxiety problem was discussed with the patient and her husband. Shortly after this visit the patient was seen by another physician near her home and given sustained released phenobarbital 1½ gr. twice daily and ethchlorvynol, 500 mg. at bedtime. The patient was next seen on June 20, 1958, and stated she was feeling fine on the above program. She was advised to continue on the same medication.

On Aug. 4, 1958, the patient returned to the office complaining of dizziness, increased nervousness, and unsteadiness. She stated that the dizziness began about two weeks before this examination and fluctuated from time to time. She denied nausea or vomiting but had noticed

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her gait seemed unsteady, with a tendency to stumble. She denied muscle weakness or paresthesias. Physical examination revealed a blood pressure of 110/70, pulse 90, temperature 98.6° F. There was a grade 2+ tremor of the hands, gross horizontal nystagmus bilaterally, and decreased tendon reflexes in both lower extremities as compared with previous examinations. Coordination was poor on finger-to-nose testing, straight-line walking was poor, and the Romberg test was positive. Sensation was normal and there were no abnormal reflexes. The rest of the physical examination was normal.

The patient was admitted to the hospital for further study. Laboratory examination revealed a normal urinalysis, a hemoglobin of 12.5 gm. percent, white blood count of 6,600 with a normal differential, and a hematocrit of 41. The serology was nonreactive. Spinal fluid examination showed a pressure of 80 mm. of water, 2 red blood cells, and 0 white blood cells per cu. mm. The protein was 36 mg. percent, and the colloidal gold curve was normal. The skull and chest X-rays were normal. An ophthalmology consult reported both horizontal and vertical nystagmus with normal fundoscopic and visual field examination. Caloric tests gave a normal response bilaterally. Within thirty-six hours after admission to the hospital the patient experienced a complete remission of her symptoms. Her only medication was promazine hydrochloride 50 mg. intramuscularly the night of admission and sustained action phenobarbital twice daily, 1½ gr. She was discharged on the third hospital day with a normal physical examination. The nystagmus, decreased coordination, dizziness, and unsteadiness were gone. The reflexes, Romberg test, and straight-line walking were normal. The diagnosis was anxiety neurosis, with possible labyrinthitis or multiple sclerosis.

The patient did well after discharge until October 1958 when she again noticed onset of nervousness and hyperventilation attacks. She resumed her sustained action phenobarbital 1½ grains twice daily and the ethchlorvynol, 500 mg. at bedtime. On Oct. 21, 1958, she was examined because of recurrence of unsteadiness and dizziness. At this time she again demonstrated horizontal nystagmus and unsteadiness with poor coordination. She was asked to stop all medications and was given diphenhydramine hydrochloride 50 mg. 3 times daily. She was examined again on Nov. 25, 1958, with identical findings and continued on the above medication. On Dec. 31, 1958, she was readmitted to the hospital because of marked increase in unsteadiness, staggering, and a speaking difficulty. She complained of dull frontal headaches in the last few weeks. Physical examination showed a blood pressure of 110/70, pulse 96, and temperature 98.6° F. The examination was normal except for the neurological examination. The speech was halting and stuttering, there was vertical and horizontal nystagmus, the gait was very ataxic, and she could walk only with help. There was bilateral impairment of coordination as measured by the finger-to-nose and heel-to-shin test. The knee jerks and ankle jerks were absent; however, the biceps reflex was present. Sensation was normal and there were no abnormal reflexes. Laboratory examination disclosed a normal urinalysis with a specific gravity of 1.022, no albumin, no sugar, and negative microscopic data. Hemoglobin was 12.7 gm. percent, and the white blood count was 4,550 per cu. mm. with a normal differential. The fasting blood sugar was 85 mg. percent, the CO_2 combining power was 20.7 mEq., the serum calcium was 10 mg. percent, and the protein-bound iodine was 5.5 μg. percent. Skull X-rays were normal. The patient was given the diphenhydramine hydrochloride 50 mg. 3 times daily and ethchlorvynol 500 mg. at bedtime. By the second day after admission the patient showed marked improvement. The speech was perfectly normal and she was able to walk easily and do some straight-line walking. The nystagmus was practically gone. At this time the ethchlorvynol was discontinued and secobarbital sodium, 1½ gr. given at bedtime. After stopping the ethchlorvynol the patient seemed to become more nervous. On the third hospital day she had a normal neurological examination but was very nervous and agitated. At this time she was begun on promazine hydrochloride, 50 mg. intramuscularly every four hours. Close questioning of the family and the patient at this time revealed that the patient had been taking 10 to 15, 500-mg. capsules of ethchlorvynol daily during the period immediately preceding both hospital admissions, and somewhat lesser amounts at other times when she demonstrated the unsteadiness and nystagmus. On the fourth hospital day the patient was intensely nervous, pacing the floor, and the promazine hydrochloride was discontinued. She was given secobarbital ¾ gr. every four hours as needed for agitation. At 9:30 p.m. on the fourth hospital day the patient had a seizure with loss of consciousness and clonic convulsions of the entire body lasting approximately two minutes, followed by a period of confusion associated with twitching and hyperactivity. At this time the patient was rebegun on ethchlorvynol 200 mg. every two hours for nervousness and diphenylhydantoin 1½ gr. 3 times daily. The

patient had 3 grand mal seizures on the fifth hospital day associated with visual and auditory hallucinations. Repeat spinal fluid examination was normal. The patient was given ethchlorvynol 200 mg. every four hours for the next three days. Her hallucinations cleared and she had no further seizures. The ethchlorvynol was discontinued on the eighth hospital day and she was treated with meprobamate 400 mg. four times daily. A neurological examination on the fourteenth hospital day was completely normal and the patient was discharged on the twenty-sixth hospital day under psychiatric care. The patient has been seen since at intervals of approximately six months and has remained well. She was discharged from psychiatric care after four months of therapy and, although she admits having tension problems, is on no medication. When last seen on November 15, 1963, she had had no symptoms, had never had any further seizures, and felt well. She weighed 130 lb. and the physical examination was normal.

DISCUSSION

Ethchlorvynol is a nonbarbiturate hypnotic sedative that is widely used as a tranquilizer and hypnotic.[9,10] Ethchlorvynol is a tertiary alcohol and has been felt to be a stronger central nervous system depressant than chlordiazepoxide hydrochloride and hydroxyzine hydrochloride[10] with minimal side effects.[11] In a series of 13 patients with ethchlorvynol ingestions, McKown[8] found that 9 persons required hospitalization and in 2 patients coma occurred. Side effects as listed by Abbott Laboratories in a study of 1,550 cases of placidyl for insomnia and daytime sedation were nausea, 8 cases (0.52%); vomiting, 3 cases (0.19%); syncope, 9 cases (0.58%); dizziness, 63 cases (4.1%); hypotension, 3 cases (0.19%).[12]

The case presented here illustrates some of the present day problems in the use of tranquilizing drugs generally. Control of the patient, particularly the patients with psychoneuroses who are likely to require sedation, is difficult. Both accidental and intentional overdose can occur. The frequency of complaints of dizziness and ataxia in patients on ordinary doses of ethchlorvynol is interesting in view of the marked vestibular symptoms illustrated by this case. Even more of a problem than overdosage with intoxication, however, is the problem of habituation and addiction. In general the salient differential point between habituation and addiction has been the absence of the abstinence syndrome in habituation.[13] Under drugs associated with physical dependence Seevers[14] has listed the following in order of magnitude of abuse: (1) alcohol, (2) morphine-like analgesics, and (3) barbiturate-like sedatives. The primary difference in acquisition of physical dependence between the morphine-like analgesics, alcohol, or barbiturate-like sedatives is that the latter require a long period of poisoning with large doses in order to produce physical dependence. This certainly existed in the case presented here. The exact dose of ethchlorvynol can only be approximated in this patient as it varied from time to time. However, there is no question that the dose was excessive and maintained over a period of time.

Use of the tranquillizer group of drugs requires an accurate knowledge of the multiple side effects and diverse manifestations of toxicity that can occur. The toxic effects on the central nervous system even in ordinary doses by chlorpromazine, reserpine, and prochlorperazine are well known.[15] The allergic or toxic effects of the above agents plus meprobamate are watched for by the alert physician.

Study of the case presented here suggests that ethchlorvynol closely simulates barbiturates and meprobamate. Like meprobamate, ethchlorvynol appears to have a larger margin of safety than barbiturates comparing the doses required for sedative and toxic effects. It would seem apparent, however, that as with meprobamate and barbiturates the development of habituation and the occurrence of abstinence reactions can occur. It would seem that the same degree of caution in prescribing barbiturates be applied to tranquilizers, more particularly meprobamate and ethchlorvynol. Patients should be cautioned against prolonged treatment and any change in dosage.

SUMMARY

A case is presented demonstrating the development of marked neurological abnormalities due to chronic overdose of ethchlorvynol and the occurrence of a severe abstinence reaction after withdrawal of the medication. It is concluded that prescribing ethchlorvynol deserves the same careful management and caution used in the administration of the barbiturates and meprobamate.

Drugs Used

Generic Name	*Trade Name*
ethchlorvynol	Placidyl
prochlorperazine	Compazine
promazine	Sparine
diphenhydramine	Benadryl
meprobamate	Miltown, Equanil
chlordiazepoxide HCl	Librium
hydroxyzine HCl	Atarax, Vistaril

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CONSERVATIVE SURGERY can produce good results in endometriosis. When definitive surgery is required, total hysterectomy with preservation of ovarian function usually is adequate. If childbearing is desired, local resection of gross endometriosis provides a reasonable chance for pregnancy, even though additional treatment may be required eventually. A five-year follow-up study was made after operation in 79 patients with endometriosis. Total hysterectomy with ovarian conservation was performed in 40, and only 1 required subsequent treatment. Local resection with preservation of the uterus was performed in 39, and 13 required additional surgery; 14 of the 36 married patients became pregnant 31 times.

JOSEPH L. SHEETS, M.D., RICHARD E. SYMMONDS, M.D., and EDWARD A. BANNER, M.D., Mayo Clinic and Foundation, Rochester, Minn. Obstet. and Gynec. 23:625-628, 1964.

SURVIVAL AFTER INITIAL TREATMENT of breast cancer is not significantly different whether castration is done at the same time as operation or later when metastasis or recurrence takes place. Early prophylactic castration prolongs the period between initial therapy and onset of recurrent disease, but survival is brief after recurrence. The time between recurrence and death is extended by late castration, but total survival time is not significantly different. Analysis was made of 119 patients with early and 177 with late therapeutic castration.

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Immunity to Tuberculosis as Revealed from Studies of Tuberculosis in Nurses

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THIS SERIES of papers honoring the late Dr. J. J. Waring of Denver, Colorado, is indeed a tribute to his lifelong concern for the health of young people, especially nurses and doctors. Perhaps this was due in part to his own personal experience with the disease, first as a medical student then with final victory over it as a young doctor. Basically, however, his interest in other people's problems was Jim Waring at his best. This attitude was part of the warmth and friendliness of his nature. It was the very youthfulness of his own spirit that drew him toward young people, making their problems his own but solving them to their advantage.[1–3] To us in the East who knew him, Jim Waring was the "Grand Old Man of Rocky Mountain Medicine" but without peer in the East or West. His early interest in tuberculosis in nurses and young doctors stayed with him throughout his life. Dr. Waring remained in the front rank of progressive thinking in the new era of antituberculosis drugs as he had been in the days of empirical therapy.

The history of tuberculosis has clearly outlined 4 mileposts in the long struggle for its control. The first of these was obviously the discovery of the tubercle bacillus by Koch in 1882 with his development of the intradermal skin test indicative of underlying tuberculous infection.

The second great discovery was that of X-ray photography by Roentgen in 1895. It was by the merest chance, although the mark of true genius, that Roentgen discovered the greatest of all diagnostic aids for an enormous variety of diseases, but especially pulmonary tuberculosis. It was in 1895, apparently in December, seventy years ago, that this historical landmark took place. Roentgen, while experimenting with a highly exhausted vacuum tube on the conduction of electricity through gases, noticed by chance that some crystals of barium platinocyanide scattered on a paper screen nearby became brilliantly fluorescent while the current passed through the vacuum tube, even though the visible light was completely screened by a black mantle over the tube. From this chance observation, he constructed the complicated basic fabric of modern X-ray photography.

The third accomplishment was the eradication of bovine tuberculosis in cow's milk through efforts of the Bureau of Animal Industries by the United States Public Health Service. This exciting saga has been well documented by Myers[4] and deserves to be reread by all those interested in the eradication of tuberculosis in human beings. He points out how cattle, positive to the tuberculin test, were removed from herds and slaughtered but compensated for by state and federal agencies. The rest of the herds were protected from infection. Although pasteurization of milk began in 1900, tuberculin testing of cattle was not seriously undertaken until 1909, with the sole purpose of eradication of the disease in cattle as an objective. At that time some herds were infected with tuberculosis up to 20% or more. By 1925 no infected cattle could be found where intensive efforts had been carried out, as in Washington, D.C. Now, due to complacency, tuberculosis in cattle is again a problem requiring new and more intensive efforts if it is to be truly eradicated. The parallel with human tuberculosis is indeed close.

The fourth and probably the greatest milepost in the history of tuberculosis control was the dis-

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covery of antituberculosis drugs—first streptomycin by Waxman in 1948 and then isoniazid and para-aminosalicylic acid, with others to follow, well outlined by Hinshaw and Riggins.[5]

However, were it not for the numerous meticulous studies of tuberculosis in nurses in the 1930s and '40s, there is much that would never have been known about this disease and its natural history in man. Experimental animals have clarified many facets concerning the nature of tuberculosis, but in man alone do we encounter the problems that man must treat.

Dr. J. Arthur Myers, who asked me to write for this series concerning tuberculosis in nurses, should preferably have done so himself. The real pioneer work in this field was done by him, and in 1930 before other publications on the subject had been started Dr. Myers wrote widely on the natural history of tuberculosis in infants,[6] among boys and girls,[7,8] among adults,[9] in the aged,[10] and in nurses.[11,12] His observations concerning primary tuberculosis infection and many other of his observations in those early days of unsophisticated attitudes toward tuberculosis have stood the test of time. He pointed out many times that "prevention in tuberculosis is prevention of exposure to the tubercle bacillus" and "protection from exposure" is still the basis of our programs for eradication today. In these days of the eradication concept, we would do well to remember his warning then[8] that "the tubercle bacillus can be subdued and held in abeyance only by constant warfare." Perhaps this observation should serve as a reminder wherever complacency creeps into attitudes toward tuberculosis today. Over the years Dr. Myers has undoubtedly done more than any other physician for the protection of our nurses and young doctors[11–14] presenting the evidence that demonstrated the great risks of exposure to the bacillus. This work was started in 1920[12] with only routine examination of those nurses with presenting symptoms. It became clear by 1927, however, that the attack should be made on the tubercle bacillus itself rather than on the damage it had done. He used conversion of the tuberculin test from negative to positive as the only index of primary tuberculosis. Dr. Myers' faith in the tuberculin test has never wavered, and then in 1927 he clearly pointed out that the tuberculin-positive individual was, of course, the only one who could develop manifest tuberculosis. He compared the infection rate in nurses in 1934[11] with that of the general population one hundred years before in the same area. He showed clearly how antiquated was our attack upon this highly infectious disease, even in areas where it should be most easily controlled—in our own hospitals and nursing schools. The example of eradication in cattle he stresses again later in 1963,[4] believing that eradication in human beings will come only through meticulous tuberculin testing community by community. Proper treatment of patients with active cases and their contacts, with prophylactic treatment of tuberculin converters to positive, was necessary. One hundred years more, he believes, will be needed to complete the task of eradication. Dr. Myers is much more honest and realistic about eradication than most of our "crystal gazers."

The subject, tuberculosis in nurses, is really no more than a jumping-off point in this discussion, for to these girls we owe a great debt of thanks for their contribution to our basic knowledge of this disease. Their cooperation and willingness to be carefully studied have clarified the clinical nature of tuberculosis as it has been observed over the three years of training characterized by hard work and high exposure to a dangerous, infectious disease. It is true that these observations on tuberculosis in nurses were begun primarily for their protection, but it soon became apparent that herein lay serial observations not previously recorded but possible only in such a "captive" group under constant observation and living under very uniform conditions.

In reviewing reports from across the country, there has been some conformity in spite of individual differences. In general, a little more tuberculosis has appeared among those nurses whose skin tests were tuberculin-negative on admission to training, compared with those whose tests were positive. But this in a way is a logical result. Among those exposed and converted as tuberculin reactors sometime before admission to training, some, especially the more susceptible, must have developed their active disease before the choice of a nursing career became necessary. Therefore, these individuals with tuberculosis were eliminated before they could apply for training. Others converted but did not develop clinical disease until the rigors of training caused them to break down or new recurrent exposure was more than they could handle. On the other hand, the nonreactors to tuberculin on admission offered virgin soil for the tubercle bacillus. Differences in results in different parts of the country were probably accounted for by the risk of infection and the severity of disease contacted. Geer in 1934[15] in St. Paul showed nearly 4 times as much tuberculosis in the converters to positive while in training. Shipman and Davis,[16] on the other hand, in San Francisco, showed most of their tuberculosis developing in the tuberculin-

positive reactors on admission. Most of these nurses' tests, negative on admission, were negative on completion of training. Thus, their preventive techniques were very good or there was very little open, active tuberculosis on their wards and, therefore, a minimum danger of contact. Badger and Spink in 1936[17] in a preliminary study showed most of their cases in those patients who were initially nonreactors, but there were some twelve thousand hospital days a year of active tuberculosis on the Boston City Hospital wards in those days, and the risk of exposure was high and the group was small. Pollack and Cohen[18] showed 20 times as much tuberculosis in their nurses as was seen in New York Telephone and Telegraph workers and 4 times as much as in Metropolitan Life Insurance workers, a terrific condemnation of the risk for nurses. On the contrary, Amberson and Riggins at Bellevue in 1936,[19] where active tuberculosis was plentiful, found tuberculosis no more prevalent than that expected among young women in other occupations in New York City. Studies in 1941 of a fifteen-year follow-up of 745 nurses at the Boston City Hospital showed essentially the same amount of tuberculosis in those nurses who initially reacted positively and negatively.[20]

So variations in conclusions across the country and abroad have evened up on the whole, to bear out Dr. Myers' early contention that tuberculosis develops only in those with a positive tuberculin test but that the nonreactors must be watched closely.

Today, the pathogenesis and natural history of tuberculosis are no longer seen clinically or well known. The use of antituberculosis drugs starts as soon as the diagnosis is made or suspected or an unseen primary infection is turned up by a postive tuberculin test for prophylactic medication. Therefore, little remains to observe except the visibly healing lesion or, still more nebulous, the conspicuously absent complications of primary infection, especially in children. We are familiar with the course of tuberculosis only under the influence of drugs. Concepts of predilection, susceptibility, or native and acquired resistance are lost sight of and need not even be considered in the course of successful chemotherapy. It is, however, our treatment failures that deserve a close look with reconsideration of some of these basic features of tuberculosis that may lie back of ineffective drug therapy.

Again it is the various studies of nurses that have contributed greatly to our knowledge of drug treatment failures through the insight that this closely observed and carefully studied group of young women has made possible. In our Boston City Hospital studies a few observations were of interest[20] which I will take from the text to refresh our memory concerning these important features of the natural history of tuberculosis.

The incidence of tuberculosis in initially negative and positive reactors to tuberculin. This horizontal study of tuberculosis in nurses reemphasizes certain concepts concerning the pathogenesis of the disease which formed the basis of an earlier report.[17] At that time there appeared to be few or no clinical and roentgenographic features to distinguish the tuberculosis which developed, whether it occured in reactors or nonreactors to tuberculin on admission to training. Clinically, the same type of tuberculosis was observed in both groups of individuals. The factor that seemed most important in determining the pattern of disease and the course in infection was the individual's inherent constitutional resistance to tuberculosis or her lack of it. This longer fifteen-year follow-up report substantiates those earlier observations and helps to clarify our own wavering conceptions of the pathogenesis of this disease.

The close parallelism of incidence of tuberculosis in negative and positive reactions in our nurses does not seem remarkable, although it is at variance with some other reports. It is to be expected that different results will be obtained in different hospitals, among different age groups, and in other countries. Racial as well as individual and environmental factors will influence the findings.

The reason for the high morbidity in the positive-reaction group on entry is not clear. It seems most logical to account for it on the basis of the natural history of tuberculosis in young women, for the morbidity is normally highest in this age group. Peak incidence of disease in this positive-reaction group lags behind that of non-reactors and is not at any time as high a rate. Removal of the more susceptible nurses with active cases of tuberculosis before they could apply for nursing school may account for this difference in the 2 curves of morbidity, but it seems an unimportant influence. Both groups had theoretically the same exposure to tubercle bacilli during their training, with working hours and living conditions the same. Diet was fundamentally the same, but subject to variations imposed by the idiosyncrasies of young women concerning their body weight.

Primary versus reinfection tuberculosis. The pathogenesis of tuberculosis has for many years been thought of in terms of primary or childhood-type and reinfection or adult-type tubercu-

losis, each tending to be differentiated into its own rather characteristic clinical and prognostic pattern. Tuberculin and roentgenographic surveys of children and young adults during the past twenty years have conditioned our thinking in terms of tuberculin-negative and positive reactors, again each with its own type of lesion. Primary or childhood-type tuberculosis was pictured as occurring in nonreactors whose tests turn positive and reinfection or adult-type tuberculosis as occurring in those whose tests were already positive to tuberculin. Moreover, there has been a prevailing view that primary tuberculosis is a relatively benign disease, compared with that of reinfection type.

Ghon[21] and Ranke[22] first wrote of primary tuberculosis as a childhood disease and reinfection tuberculosis as its adult form. Epidemiologic changes in the morbidity and mortality of tuberculosis have altered our attitude toward these earlier concepts, chiefly because large sections of the population now do not develop their first or primary infection until the second, third, or fourth decades of life.

Terplan,[23] in his exhaustive pathological studies of human tuberculosis, presents the evidence for primary infections up to the age of 80 years. He shows that the pattern of healed primary infections is the same for all age groups and exists in the lung parenchyma with and without regional lymphatic involvement. He feels that the development of tuberculin sensitivity should not be made the dividing line between primary and reinfection tuberculosis. Sensitivity to tuberculin occurs soon after the initial lodgment of tubercle bacilli in the body, but there is no sound basis for regarding a positive tuberculin test with the development of allergy as the criterion of reinfection.

Lurie's studies in experimental rabbits concerning the pathogenesis of tuberculosis remain among the really classical investigations into the basic science of tuberculosis, so we will continue further extrapolations of this work from the Boston study.[20]

Lurie[24] in 1944 presented the results of years of experimental study with tuberculosis in numerous strains of inbred rabbits with known variations in their inherited constitutional resistance to tuberculosis. He found that there was no constant pattern of primary or reinfection tuberculosis. Those strains of rabbits with high resistance to tuberculosis could localize the naturally acquired primary infection in the lung parenchyma without any regional lymphatic involvement. But with similar exposure, those with low natural resistance produced the familiar primary complex, with regional lymph node involvement and infection in distant organs. A single artificial infection produced similar effects and different patterns of disease which varied according to the inherent resistance of the rabbit strain when the infecting doses were similar.

Medlar,[25] in his pathological studies, found no clear-cut difference in the pathology of primary and reinfection tuberculosis in human beings. He found the primary or first infection the usual cause of death from tuberculosis under the age of 40 but, occasionally, its cause up to 60 years. Beyond the age of 40, reinfection tuberculosis was more common. The term "reinfection" tuberculosis he uses only in the sense of a new infection from outside the body: new disease acquired in the presence of a former but obsolete and healed primary infection. Thus, as Amberson points out, the differentiation of primary and reinfection tuberculosis is a pathological problem and is not possible to distinguish clinically. But Medlar goes further in his pathological studies in feeling that allergy does not play a very important part in determining the progress of the disease. He found primary and reinfection (in the strict sense) tuberculosis to be indistinguishable, on a pathological basis.

Constitutional factors. It is not clear what makes primary or first infection tuberculosis in one individual go on to subclinical healing throughout its course while in another the process becomes progressive cavernous disease and in still another it progresses from early pneumonic consolidation to a rapid death. The clinical observations of this study point to the importance of inherent constitutional resistance as being one of the most important influences in establishing the course and prognosis of each case. All our nurses had the same theoretical exposure to sputum–positive cases of tuberculosis during training and experienced similar living and working conditions. It is of importance that the initially tuberculin-negative and positive groups developed not only a closely similar amount of tuberculosis but developed disease which was clinically comparable in both groups, as seen by similar roentgenograms, treatment, and end results.

It is of interest also that of the negative reactors on admission 14% went through training without ever becoming positive reactors to tuberculin. Perhaps these individuals were endowed with a very superior resistance to tuberculosis which destroyed the tubercle bacillus before it could establish a beachhead in the body. Perhaps they were just lucky. Eighty-six percent of those who later reacted positively showed no roentgeno-

graphic or clinical evidence of tuberculosis and exhibited the presence of acquired infection only by a positive tuberculin test. Fourteen percent of those who reacted positively showed roentgenographic evidence of tuberculous lesions. In approximately a quarter of this group the lesions remained subclinical throughout the period of roentgenographically demonstrable disease. These groups must all have been endowed with good resistance to their tuberculosis.

Clinically, it has seemed to us and has been noted previously[17] that the inherent constitutional resistance of the individual to tuberculosis was the most important factor in determining the pattern of disease. Lurie[20] makes it clear from his experimental studies that "the resistance of rabbits to naturally or artificially acquired tuberculosis is a function of their genetic constitution."

Medlar[25] states that the cause for progression in some primary infections is due to inherent qualities of susceptibility of certain parts of the lung, the apices of the lobes, when infection lodges in those areas. Additive effects of frequent reexposure may lead to development of disease by the greater chance of apical involvement.

However the case may be, good mechanical technique for breaking contact and spread of tubercle bacilli should be established, but dependence upon these technical factors of prevention should not be exploited at the expense of other measures. No matter what mechanical or immunologic procedures are used in prevention, constitutional resistance, general health, fatigability, diet and nutrition, the way of living, and psychological reactions to family, work, and recreation, all play their part and contribute to the response of the host to infection.

Observations with the use of Calmette-Guérin bacillus (BCG). Comparison of our results with those of other similar studies carried on for fifteen years or more shows expected differences. Heimbeck in 1947[23] reported a twenty-year follow-up of his nurses at Ulleval Hospital.[23] His reported results are as follows.

The above figures represent the accumulated results of his group of nurses during their three-year training period only. His second period of observation includes the accumulated data of the seventeen years following completion of training. In this group it is reported that there was essentially no difference in the morbidity or mortality in the above 3 groups of nurses.

	Number of nurses	*Number of cases of tuberculosis*	*Deaths*
Pirquet positive	668	35	1
Pirquet negative (BCG vaccination)	501	42	5
Pirquet negative (No BCG)	284	105	12

The high incidence and mortality rate in his negative, unvaccinated nurses seems to indicate some racial differences in a greater susceptibility to tuberculosis in Norwegian nurses. The nurses with positive reactions on entry to training suggest a true "survival of the fit," with earlier elimination of the more susceptible by the Darwinian process of "natural selection." Their exposure to tuberculosis must have come before they reached the age for training as nurses. Again, in the unvaccinated nurses with negative reactions on entry, with their high morbidity and mortality, those susceptible to tuberculosis were eliminated under observation. Those who survived did as well in subsequent years as those who reacted positively on entrance to training. This would be expected.

This study of Heimbeck's has shown the usefulness of BCG vaccination in his nurses where results point to a racially greater susceptibility to tuberculosis and where the high morbidity and mortality suggest more severe disease and a greater risk of exposure to bacilli. The differences in results of these 2 long follow-up studies may well be explained on this analysis of racial and individual variations in constitutional factors.

In a hospital community where control against contact with the tubercle bacillus has not been elaborate but basic, it appears that many factors already outlined contribute to the development of clinical tuberculosis in addition to contact with the microorganisms. It is not enough to consider the individual lesion alone during the time a nurse is in training. In this study the detailed analysis of the progress of the disease is considered in the light of further understanding the pathogenesis of tuberculosis from clinical experience. The perspective granted by the fifteen-year follow-up emphasizes the excellence of late results and the importance of the inherent constitutional capacity of young women to handle tuberculous infections successfully, when diagnosed and treated in the earliest stages.

A discussion of primary or reinfection tuberculosis has led us to the conclusion that most, if not all, of the disease in this group has been primary, first infection tuberculosis, whether it appeared in the initial reactor or nonreactor to tuberculin.

These studies have shown that the first infection, or primary tuberculosis, as seen in the initially negative tuberculin reactors, may go on to progressive destructive tuberculosis of almost any type. It may, in the other extreme, become

rapidly arrested, with clearing of the shadow on the roentgenogram, and at no time give constitutional or local signs or symptoms of clinical tuberculosis. All gradations of the disease may appear between these extremes. The tuberculosis which appeared in the initially positive reactors acted in the same manner. Thus, the state of allergy appears to play less part in the pathogenesis of the disease than do inherent constitutional differences in resistance to tuberculosis, with environmental factors and treatment.

With this background of experience gained in the days before modern drugs, it is fair to say that it is difficult, if not impossible, to ferret out at first examination those who will do well and those who will not, those who have good native resistance and those who lack it. Time alone will tell. If, however, we are dealing with an initial infection with the human bacillus and not an atypical organism or one shown to be resistant to the common drugs, we will expect 95% or more to do extremely well with drug treatment, while a few will improve more slowly and an occasional case will be progressive.

What are the factors of predilection unrelated to drug resistance of the organism that lead to failures of modern drug treatment? Inherent constitutional susceptibility and resistance cannot be measured except by suspicion based on the presence or absence of a family history of tuberculosis. Even racial differences are looked upon askance today until overall living conditions, the type of nutrition, the occurrence of famine in developing countries or in overcrowded city slums, and the intercurrent wasting diseases are considered.

Dr. Rene Dubos in his 1964 Amberson Lecture at the annual meeting of the American Thoracic Society showed clearly that the effectiveness of BCG vaccination was tremendously vitiated in countries where starvation and inadequate diets brought malnutrition. The same was shown to be true of isoniazid, where its effectiveness as treatment and prophylaxis was diminished if malnutrition existed.

It is of interest that some years ago in the great Philadelphia Aviary large numbers of birds died of tuberculosis. Quite unsuspecting, a dietary change, high in protein, saw almost complete elimination of the disease in a few years. Review of earlier diets for the birds showed a greatly deficient protein content. This unscientifically planned observation, this dietary error, was perhaps a stroke of genius in the evidence of effects upon alterations in susceptibility.

Surgery may affect the constitutional suceptibility unfavorably in the nutritional changes following subtotal gastrectomy.[26] Corticosteroids will lower resistance to infections of all kinds, including tuberculosis. Certainly those individuals with known tuberculosis or suspected lesions who must remain on corticosteroids for a long time should receive prophylactic isoniazid. It is not yet clear and will not be until a well-organized control study is carried out whether all those with tuberculin-positive reactions who are on corticosteroids should also receive isoniazid. But where the family history shows much tuberculosis, where intercurrent wasting disease occurs, or where known contact with open tuberculosis is a high risk, probably then the positive reactor on long-term steroids should be given prophylactic isoniazid.

BCG in nurses. The long and arduous controversy over the value of BCG in nurses will not be dealt with in detail. Hennebeck[27] in Oslo, Norway, was the first to try this. His studies were confused by a perplexing protocol and his results in the long run not so different from our own.

The United States Public Health Service started a large cooperative study of the use of BCG in nurses in this country, but it was given up after a few years. The reasons for discontinuing it are not clear to me. I suspect from other publications[28,29] that the use of BCG was not of significance and that the discontinuance may have been justified. The impression exists, however, that with the nurses as with other groups the use of the tuberculin test as an index of primary infection with the tubercle bacillus was considered more important than efforts at prevention with BCG. In other words, the conversion rate from negative to positive reactions was sufficiently small to be handled better and more surely by prophylactic treatment with isoniazid.

Again, in the Boston City Hospital analysis of our BCG-vaccinated nurses,[30] there was seen the same rate of active clinical tuberculosis in the BCG-vaccinated as in those tuberculin-positive patients on admission. This was more or less to be expected, however, as BCG, if it works, should approximate rates in those who have tuberculin-positive reactions by contact. This study, with the BCG administered by the Massachusetts Public Health Department, demonstrated that our tuberculin testing program was no longer of any use, since all the negative reactors on admission were made positive artificially. This in reality is the decision that must be made: a case-finding program dependent on the use of BCG or the tuberculin test as an index of the absence or the presence of infection for treatment or prophylaxis. The tuberculin test or BCG can be used in the same institution or community.

The penalties of vaccination have been outlined by Palmer[28,29] in 2 large-scale studies. He pointed out also the vitiation of the tuberculin test as a useful tool following the use of BCG, the impossibility of differentiating the sensitivity conferred by BCG from that due to the tubercle bacillus, and the interference with the use of the tuberculin test for epidemiologic study. These things he points out are important considerations in countries and communities where the number of reactors is so small that they can be kept under surveillance. The value of the tuberculin test increases, he notes, with the lower incidence of positive reactors.

There has been accord, in general, that among our nurses and young people periodic tuberculin testing, with careful follow-up of those with positive reactions with chest X-rays and periodic retesting of those with negative reactions and those with positive contacts, is the control program of choice.

Overconfidence that eradication is just around the corner and an acquired complacency in the effectiveness of control have weakened our defenses, and tuberculosis in 1963 was seen to be on the increase in some of our major cities at a forbidding rate. Perhaps the use of BCG in certain high incidence areas in this country will require reexamination if present rate increases continue. New York City has already adopted the use of BCG this year in some 20,000 school children in areas where follow-up is difficult and poverty and overcrowding persist. It may be, as the incidence of nonreactors increases and the virgin field for primary tuberculosis infection spreads, that great need may arise for the wider use of BCG against tuberculosis. However, perhaps a new, more stable, and more effective vaccine than BCG may be found to offer the protection against tuberculosis that we have in an increasing number of vaccines for protection against other types of infection. It has been clearly noted, however, that drugs and BCG or other vaccines are good only up to a certain point. Thereafter, more subtle influences work for or against our well-laid plans.

It has been the purpose of this paper to use tuberculosis in nurses as a launching pad for generalizations concerning the more obscure and less well-recognized factors that lead to failures in treatment as well as to a better understanding of factors that affect our native and acquired resistance to tuberculosis over the long haul of a life-span. The specifics of drug treatment, so well known to all, have been sidestepped. Rather, have we given thought to the basic concepts of the natural history of tuberculosis that modern drug therapy has camouflaged. Heredity, constitution, and predilection will continue to play an important role in the eradication of tuberculosis. Let their influence be ever in mind and never be overlooked in our long and arduous battle against this tough and rugged tubercle bacillus.

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Henry W. Woltman, M.D.

A Memorial

JAMES ECKMAN, Ph.D.
Rochester, Minnesota

DR. HENRY W. WOLTMAN, one of the foremost neurologists in the United States, and a member of the staff of the Mayo Clinic from 1919 to 1956, died of cardiac arrest due to calcific aortic stenosis at the Worrall Building of the Rochester Methodist Hospital at 3:30 p.m. on Nov. 27, 1964. Dr. Woltman had been in the emeritus staff rooms of the Mayo Clinic when he suddenly collapsed, and he died shortly after he had been admitted to the hospital. He had retired from active practice in 1956.

From the time of his first paper on tremors, reflexes, and muscular spasms, published in 1917, until his retirement Dr. Woltman concentrated his attention on neurology, and he early became recognized as an international authority in this field. He was especially known for his studies in polyneuritis and for his work with diverse forms of neuritis.

Dr. Woltman was born on June 16, 1889, at Westfield, Wisconsin, the son of Elizabeth Prack Woltman and Henry L. Woltman. He received the degree of bachelor of science from the University of Minnesota in 1911 and that of doctor of medicine from the same institution in 1913. At the University of Minnesota he was a classmate and close friend of Dr. Frederick P. Moersch, also a neurologist, who retired from the Mayo Clinic on April 1, 1956.

From April 1, 1913, to June 30, 1914, Dr. Woltman was an intern in the University of Minnesota Hospitals. From 1914 to 1917, he was a teaching fellow in neurology and psychiatry in the University of Minnesota Medical School, and from 1917 to 1919 he was a first lieutenant in the Medical Corps, U.S. Army. He came to Rochester, Minnesota, on July 1, 1917, as a first assistant in neurology from the University of Minnesota. He became an instructor in neurology in the Mayo Graduate School of Medicine, University of Minnesota, in 1918. He was appointed to the staff of the Mayo Clinic in 1919. He became assistant professor of neurology in 1920, associate professor in 1922, and professor in 1931.

Dr. Woltman was appointed head of the Section of Neurology and Psychiatry in the Mayo Clinic on April 1, 1930. From 1947 to 1954 he served as chairman of the Sections of Neurology and Psychiatry in the Mayo Clinic, and became a senior consultant in 1954. Dr. Woltman would have retired from active practice in 1954, but unusual considerations at that time within the Mayo Clinic made it desirable for him to continue as a special consultant in neurology, a post which he accepted and in which he served until July 1, 1956.

Dr. Woltman was certified as a specialist in psychiatry and neurology by the American Board of Psychiatry and Neurology, Inc., in 1935. He was one of the founders of this board, and was a director, 1937 to 1941, and vice-president in 1940.

Dr. Woltman was president of the Minnesota Society of Neurology and Psychiatry and of the Central Neuropsychiatric Association in 1937, of the Association for Research in Nervous and Mental Diseases in 1948, and of the American

JAMES ECKMAN *is with the Section of Publications, Mayo Clinic, Rochester.*

Neurological Association in 1950. He was president of the staff of the Mayo Clinic in 1946, and he was a member of the Advisory Council of the National Institutes of Neurological Diseases and Blindness, U.S. Public Health Service, and Medical Advisory Committee of the National Foundation for Infantile Paralysis. He was chairman of the Section on Nervous and Mental Diseases of the American Medical Association in 1934, and was secretary of that section in 1931, 1932, and 1933. He was an area consultant to the Veterans Administration, and served as president of the Mayo Foundation chapter of the Society of the Sigma Xi.

Dr. Woltman also was a fellow of the American College of Physicians, the American Academy of Neurology, and the American Medical Association, and a member of the American Psychiatric Association, the Central Society for Clinical Research, the Alumni Association of the Mayo Foundation, the Society of the Sigma Xi, the Alpha Kappa Kappa professional medical fraternity, the Chicago Neurological Association, the American Neurological Association, and the Alpha Omega Alpha medical honor society. He was a senior honorary member of the Medical Advisory Board of the National Multiple Sclerosis Society.

He had contributed extensively to neurologic literature, particularly on the neurologic changes associated with pernicious anemia and neuritis.

On Oct. 16, 1954, Dr. Woltman, with Dr. Frederick P. Moersch, was honored by a special celebration held by his colleagues and former students in Rochester. A special portrait of Drs. Woltman and Moersch, made by Yousuf Karsh, of Ottawa, Canada, was unveiled and presented to the 2 men, and it was announced that a forthcoming volume, *Clinical Examinations in Neurology,* by members of the Section of Neurology of the Mayo Clinic, would be dedicated to them. The volume was published in 1956.

In 1957 Dr. Woltman received an award for outstanding achievement from the University of Minnesota, and in 1958 he was appointed chairman of the Olmsted County Mental Health Advisory Board, which he previously had served as vice-chairman. He served as chairman until 1960. In 1958 he also made a tour of medical facilities in Russia as a consultant to the U.S. Public Health Service. In 1963 he was the recipient of a special award from the Minnesota State Medical Association in recognition of his attainment of fifty years in the practice of medicine.

In interests outside his profession Dr. Woltman was known as a highly skilled lapidary, and he sectioned, polished, and mounted many native stones, particularly agate and other local varieties. He had a keen interest in the geology of Minnesota, and also was recognized as an accomplished woodworker.

Dr. Woltman married Mildred Bertie, of Forest Hills, Long Island, New York, on Oct. 25, 1917. Mrs. Woltman and 4 children survive: Mrs. Audrey Endress, of San Francisco, California; Henry of Saint Paul, Minnesota; David of Rochester, Minnesota; and John of Stillwater, Minnesota.

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Book Reviews . . .

Blood Diseases

by M. A. ATAMER, *616 pp., ill., Grune & Stratton, New York, 1963. $16.50*

This book covers the broad field of blood disorders, including abnormalities of clotting and the anemias. However, in attempting to span the entire field of hematology, the author has found it necessary to cover each disorder in a rather superficial fashion. The discussions of each disease are generally broken down into a definition and sections of physiopathology, clinical laboratory manifestations, diagnosis, prognosis, pathology, and treatment. Some statistical data are given in the form of tables; however, there are no photographs or other illustrations presented. This would seem to be a very definite defect, particularly in a text discussing hematology, where illustrations are very important in the understanding of the disease process. Each section has ample references listed so that the reader can go to original source material.

In general, I found the field of hematology to be covered very well but not in great depth. Many of the controversial aspects of the various blood diseases are not discussed, and the material is presented in a didactic fashion. The book will be most useful to medical students and practitioners who have only occasional involvement with patients who have hematologic disorders and who do not have great interest in this field. It should make a useful addition to the desk of the practicing physician where it can be used for a quick reference.

ALVIN L. SCHULTZ, M.D.
Minneapolis

Physiological Problems in Space Exploration

edited by JAMES D. HARDY, *333 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $12.50*

This is the latest of a half-dozen books appearing in the past two years that discuss the biologic and medical challenges to space travelers. This book has the special virtue of incorporating among its total of 9 chapters 3 beautiful ones prepared by its eminent editor, who is director of the John B. Pierce Foundation Laboratory at Yale. These 3 chapters cover temperature, acceleration, and weightlessness aspects of getting along in space. The remaining 6 chapters cover ionizing radiation factors in space, the gaseous intraspacecraft requirements, food in space (including a very interesting discussion of food in its role as "the oldest tranquillizer" and the most widespread "addictor" leading to obesity), sensory organ functions in space flight, and mental considerations during prolonged isolation and confinement. Also, biologic rhythms, certain of which tend to be synchronized with the solar day-night cycle, are discussed in some detail. All of the authors are outstanding authorities, and this 322-page volume represents considerable effort on their part to include key information without undue detail.

The only shortcoming this reviewer finds with the book is a minor one: Some of the illustrations are so detailed and have been so reduced in size that they tend to strain one's eyes. The lines of print are quite legible, however, and this book is to be recommended for clinicians and medical students. For both groups it will extend knowledge of the life processes and the potential aberrations that can attend environmental extremes. It will also pro-

(Continued on page 16A)

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BOOK REVIEWS

(Continued from page 15A)

vide nutshell information on the physical nature of outer space as related to survival. Additionally, for the student and younger medical scientist, the biomedical challenges that accompany man's sojourn into the cosmos may so intrigue the mind that certain of them will seek to undertake careers in space medicine. This book is recommended as being succinct, reasonably comprehensive, and readable.

STANLEY R. MOHLER, M.D.
Oklahoma City

Craig and Faust's Clinical Parasitology

by ERNEST CARROLL FAUST *and* PAUL FARR RUSSELL, *7th ed., 1,099 pp., ill., Lea & Febiger, Philadelphia, 1964. $16.50*

This remains the most comprehensive and authoritative textbook of medical parasitology. Not only are all of the usual parasites covered thoroughly but rare and incidental forms are included. The geographic distributions are given in sufficient detail to assist the diagnostician in assessing the likelihood of infection with an exotic parasite. New illustrations, recent discoveries, and changed viewpoints have been incorporated in this edition. Thus, the ultrastructure of the malarial parasites and Toxoplasma, the possibility of human infection with soil amoebas of the genus Acanthamoeba, and the recognition of Echinococcus multilocularis as a separate species are all found here. In the treatment sections the latest drugs are given but not to the exclusion of standard remedies.

It may be presumptuous to find fault with this recognized authority, but the paragraph on the incidence of Entamoeba histolytica infection in the United States (p. 190) appears to be unrealistic. While the book states that amebiasis along with other infectious diseases has decreased, an explicit disavowal of the previously emphasized statement, that 10% of the population of the United States is infected, would be in place. The authors are more sanguine than this reviewer in their opinion that medical technologists over the country are generally competent to make accurate laboratory diagnosis of amebiasis. The replacement of figure 217, the life cycle of Clonorchis sinensis, showing a metacercaria with eyespots, is long overdue.

The illustrations are numerous and informative, the bibliographies are extensive, and the indices are complete. This book should be available to any physician who has occasion to diagnose and treat parasitic infections.

FRANKLIN G. WALLACE
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News Briefs . . .

North Dakota

DR. RALPH X. VINJE of Bismarck has been elected president of the Sixth District Medical Society. Dr. Paul F. Klosterman, Bismarck, was named president-elect and Dr. John B. Frankel, Bismarck, was elected secretary-treasurer. Featured speaker at the annual meeting was Dr. G. Alfred Dodds, Fargo, president of the North Dakota Medical Association.

* * * *

DR. KEITH G. VANDERGON, 40, has been appointed Grand Forks County health officer, replacing Dr. Theodore Q. Benson, 68, who resigned. Dr. Benson, a native of Michigan, N.D., had filled the post for twenty-eight years. He is a 1930 graduate of the University of Minnesota Medical School and has practiced in East Grand Forks and Grand Forks since 1931. Dr. Vandergon, born in Minneapolis, received his M.D. degree from the Washington University School of Medicine, St. Louis, in 1949. Following internship at Hennepin County General Hospital, Minneapolis, he practiced in Mohall for one year, in Portland, Ore., for nine years, and has practiced in Grand Forks since 1960.

* * * *

THREE NORTH DAKOTA PHYSICIANS have been elected fellows of the American College of Physicians. They are Drs. Donald M. Barnard and John L. Magness of Fargo and Dr. P. Roy Gregware of Bismarck.

Minnesota

DR. COLLIN S. MAC CARTY has been named president-elect of the Mayo Clinic voting staff. Head of the Section of Neurologic Surgery, next fall he will succeed Dr. Howard P. Rome, senior consultant in psychiatry, who assumed the presidency in November, replacing Dr. Laurentius O. Underdahl. Two staff members, Drs. John W. Kirklin, chairman of the sections of general surgery, and Charles A. Owen, Jr., head of the Section of Clinical Pathology, were confirmed as six-year members of the board of governors. Dr. Joseph M. Janes, consultant in orthopedics, was elected vice-president, Dr. Theodore G. Martens, consultant in ophthalmology, was elected secretary, and two physicians were named counselors—Drs. G. Keith Stillwell, physical medicine and rehabilitation, and Leonard A. Aaro, consultant in obstetrics and gynecology.

* * * *

DR. LAWRENCE POSTON, a 1963 graduate of the University of Minnesota Medical School, has assumed the practice of Dr. Allan D. Davidson in Caledonia. Dr. Davidson is on a three-year fellowship in ophthalmology at the Mayo Foundation, Rochester. Dr. Poston, 29, is a native of Jacksonville, Ill. He interned at Bethesda Lutheran Hospital, St. Paul, and practiced in Minneapolis before moving to Caledonia.

(Continued on page 18A)

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NEWS BRIEFS

(Continued from page 17A)

DR. DONALD M. BRINK, has closed his EENT practice in Hutchinson after twenty years. A 1937 graduate of the University of Minnesota Medical School, he has accepted a position at St. Peter State Hospital.

* * * *

DR. LADDIE E. STOVER, a general practitioner, has begun a practice in Waseca in partnership with Dr. Wayne L. Campbell. Dr. Stover was born in Duluth and received a degree in pharmacy from the University of Minnesota in 1956. Following two years as a pharmacist in Minneapolis and Portland, Ore., he enrolled at the University of Oregon and received his M.D. degree in 1962. After internship at the San Bernardino County Charity Hospital, San Bernardino, Calif., Dr. Stover practiced in Portland until moving to Waseca.

* * * *

DR. ROBERT D. SCHRANTZ of the Itasca Clinic in Park Rapids has left his practice for a residency in pathology at St. Joseph's Hospital, Phoenix, Ariz. A native of Slayton, he received his M.D. degree from the Stritch School of Medicine of Loyola University, Chicago, in 1955, and has practiced in Park Rapids since 1959.

* * * *

DR. VALENTINE O'MALLEY of St. Paul has been elected president of the Association of Minnesota Internists, succeeding Dr. Charles E. Lindemann of Minneapolis. Others elected at the annual meeting were Dr. William L. Hedrick, Edina, president-elect; Dr. Harold E. Miller, Edina, secretary-treasurer; Dr. Herbert W. Johnson, St. Paul, and Drs. William J. Paule and Albert J. Greenberg, Minneapolis, executive committee members.

* * * *

DR. DONALD F. MUHICH, of Virginia, director of the Range Mental Health Center since 1962, has resigned to become director of clinical services for the city and county of Los Angeles. A psychiatrist, Dr. Muhich practiced in San Francisco before joining the center.

* * * *

DR. BEMIS H. JOHNSTON has begun practice at the Ivanhoe Clinic in Ivanhoe. He is the community's only M.D. A graduate of Macalester College, St. Paul, he taught in Grand Junction, Colo., worked as a chemist in Salt Lake City, Utah, and received his M.D. degree from the University of Utah in 1962. Following internship in

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Duluth, he practiced in Litchfield before moving to Ivanhoe.

South Dakota

DR. WALTER E. MARCHAND has joined the Fort Meade Veterans Administration Hospital staff. He has been with the VA since 1946, first as staff physician and chief of medicine and surgery at the Veterans Administration Hospital, Bedford, Mass., and most recently with the medical staff of the Veterans Administration Hospital at Fort Bayard, N.M. Dr. Marchand, a graduate of New York University, was a battalion surgeon with the Fourteenth Infantry Division in World War II, and received numerous citations, including the Silver Star.

Deaths . . .

DR. HENRY W. WOLTMAN, a member of the Mayo Clinic staff from 1919 to 1956, died in Rochester, Nov. 27, at age 75. A neurologist, Dr. Woltman contributed many studies in neuritis and pernicious anemia.

* * * *

DR. JOHN B. MC HUGH, first director of the John Moses Memorial U.S. Air Force Hospital in Minot when it opened in 1950 as a Veterans Administration Hospital, died Dec. 12 in Wilkes-Barre, Pa. He was 57. Dr. McHugh had been director of the Veterans Administra-

(Continued on page 20A)

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WANTED: General practitioner or internist to join group of five doctors in Breckenridge, Minnesota, 5000 population. Community from which practice is drawn approximates 15,000. Age—under 35 years. Salary open with opportunity for full partnership later. Excellent 125 bed hospital. New air-conditioned building. Golfing, hunting, fishing available in area. Position open July 1, 1964. Write: Breckenridge Clinic; Breckenridge, Minnesota.

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WANTED—Pediatrician, Board eligible or qualified, to join balanced group. Write Huron Clinic, Huron, South Dakota.

WANTED—General Practitioner or internist to join 10 man group in east central South Dakota. Reply Box 26, c/o Journal Lancet.

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DEATHS

(Continued from page 19A)

tion Hospital in Wilkes-Barre since 1959. A native of Summit Hill, Pa., he received his M.D. degree from Temple University, Philadelphia, in 1934 and joined the VA in 1939, serving at 3 VA hospitals before directing the Minot hospital staff. He left Minot in 1952 for similar duties in Kansas City, Mo., before being assigned to Wilkes-Barre.

* * * *

DR. JOHN L. STENNES, 47, a Minneapolis general practitioner, died Dec. 10. Born in Haynes, N.D., he attended the University of North Dakota and received his M.D. degree from Washington University, St. Louis. Dr. Stennes was a veteran of World War II and the Korean War, as a major in the Army Medical Corps. A resident of Minneapolis since 1941, he was formerly chief of staff of Swedish Hospital, Minneapolis, and was a member of county, state, and national medical associations, and the Academy of General Practice.

* * * *

DR. LEO A. NASH of St. Paul died Dec. 1, at age 54. A roentgenologist, Dr. Nash was consultant in radiology at St. Luke's Hospital of St. Paul, and at Charles T. Miller and Children's hospitals, St. Paul, and clinical instructor in roentgen diagnosis at the University of Minnesota. He was born in Chisholm, Minn., in 1910, and received his M.D. degree from the University of Minnesota in 1935, interning at the university hospital and the Cleveland City Hospital, Cleveland, Ohio. In 1938, Dr. Nash became a fellow in roentgenology at the Mayo Graduate School of Medicine and received an M.S. in radiology from Minnesota in 1940. He was a fellow of the American College of Radiology and a member of the Radiological Society of North America, the American Roentgen Ray Society, the American Medical Association, Minnesota State Medical Association, and Ramsey County Medical Society.

* * * *

DR. AGNES D. STUCKE of Garrison, N.D., died Dec. 13 at the age of 90. In 1963 she was honored by the North Dakota Medical Association for fifty years of medical practice. A 1910 graduate of the Women's Medical College of Pennsylvania, Philadelphia, she and her husband, also a doctor, began practice in Garrison in 1911. Dr. Stucke had served for many years on the state health board.

* * * *

DR. EDWARD V. GOLTZ of St. Paul died Dec. 9, at age 84. During a long career in St. Paul, he was the first medical director of that city's Red Cross regional blood program. A 1908 graduate of the Northwestern University Medical School, Chicago, Dr. Goltz was a member of the American College of Physicians.

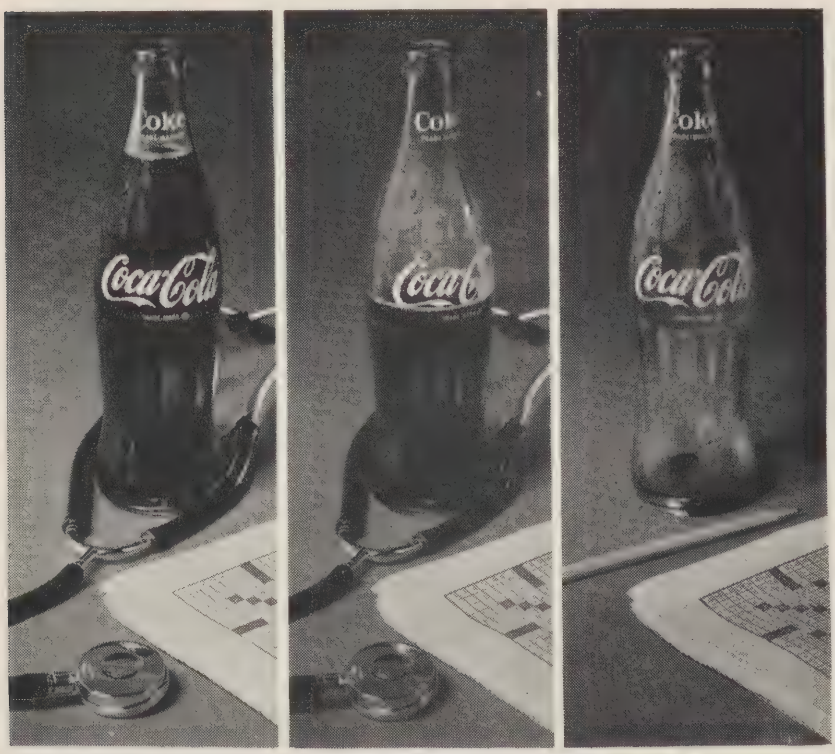
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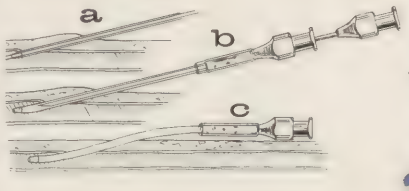
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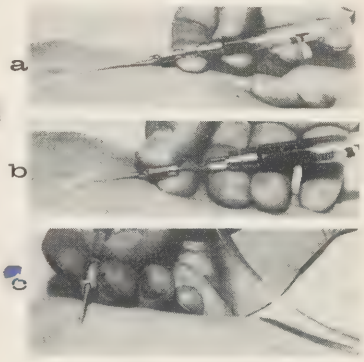
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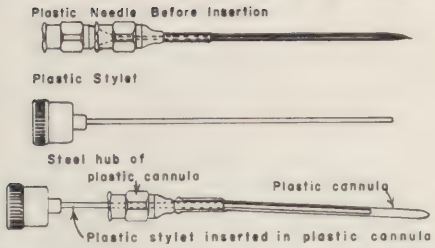




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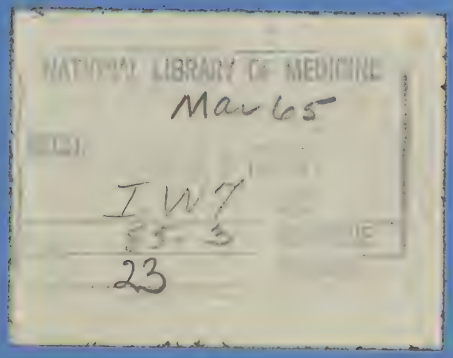
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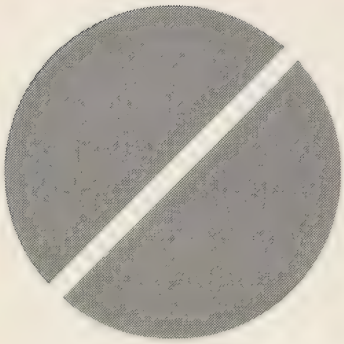
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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, *22*:527, 1964.

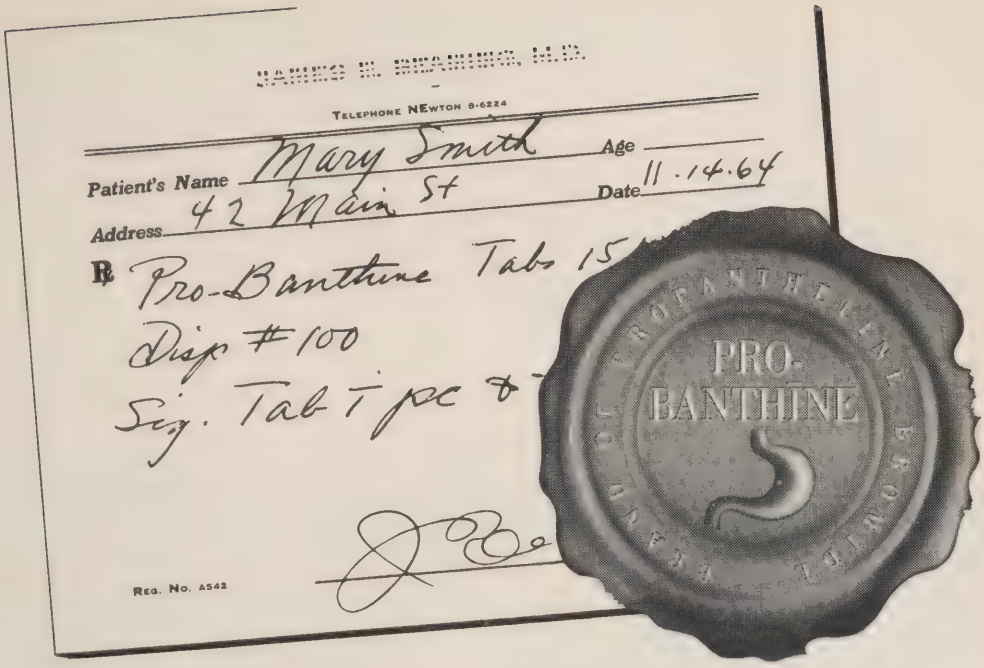
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The Journal-Lancet Volume 85, No. 3, MARCH 1965

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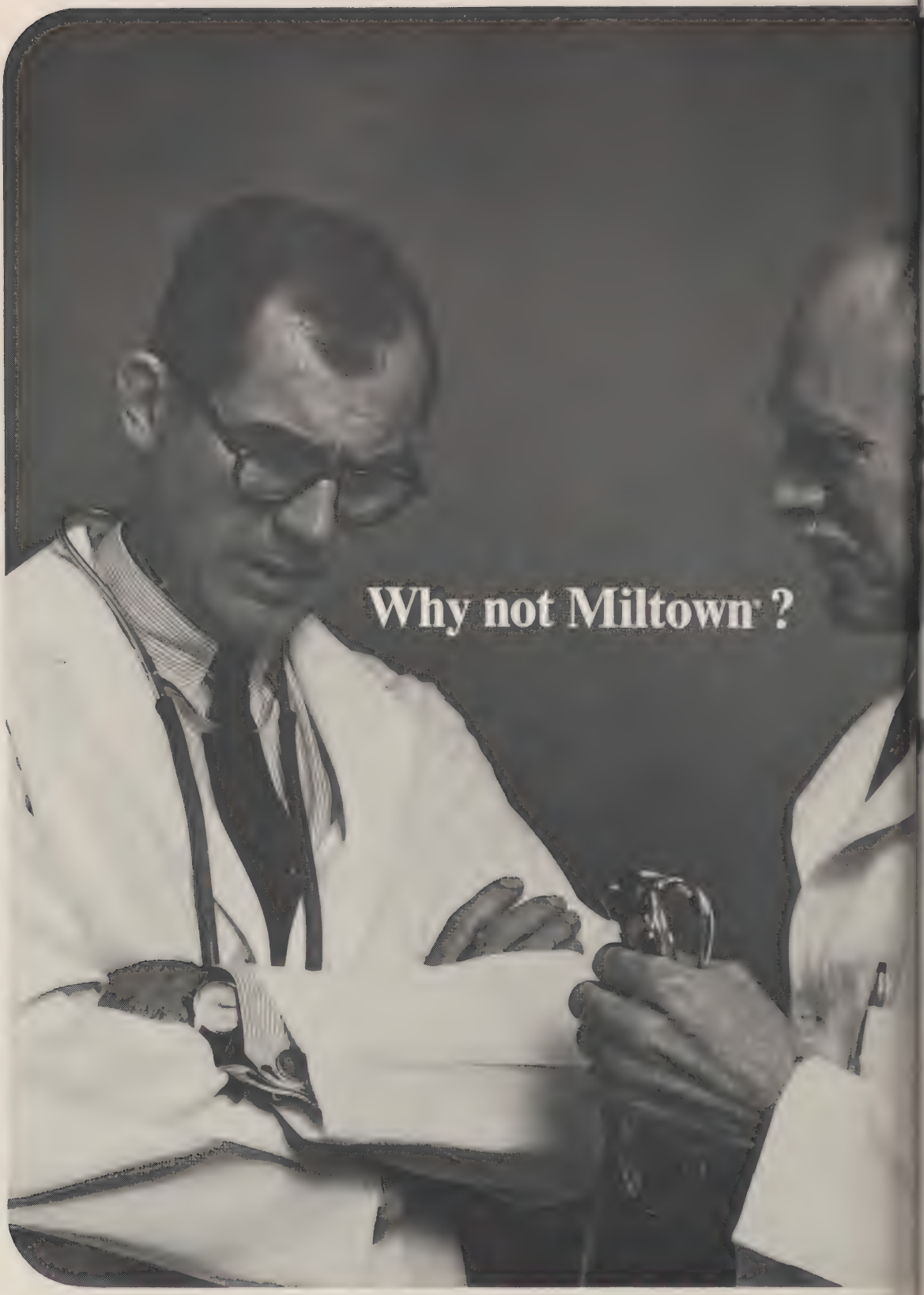
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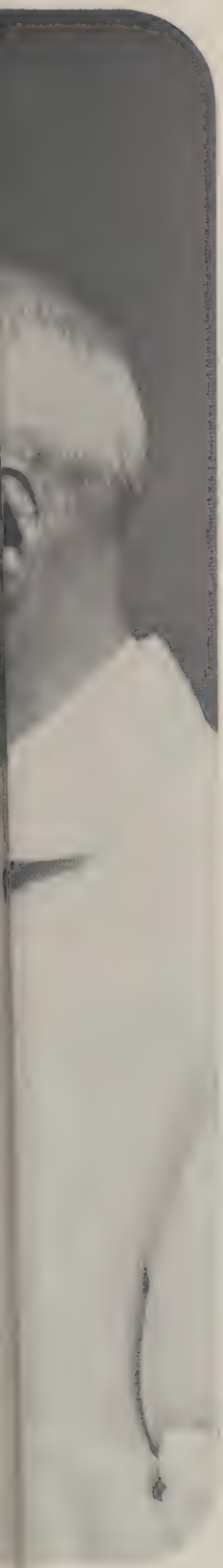
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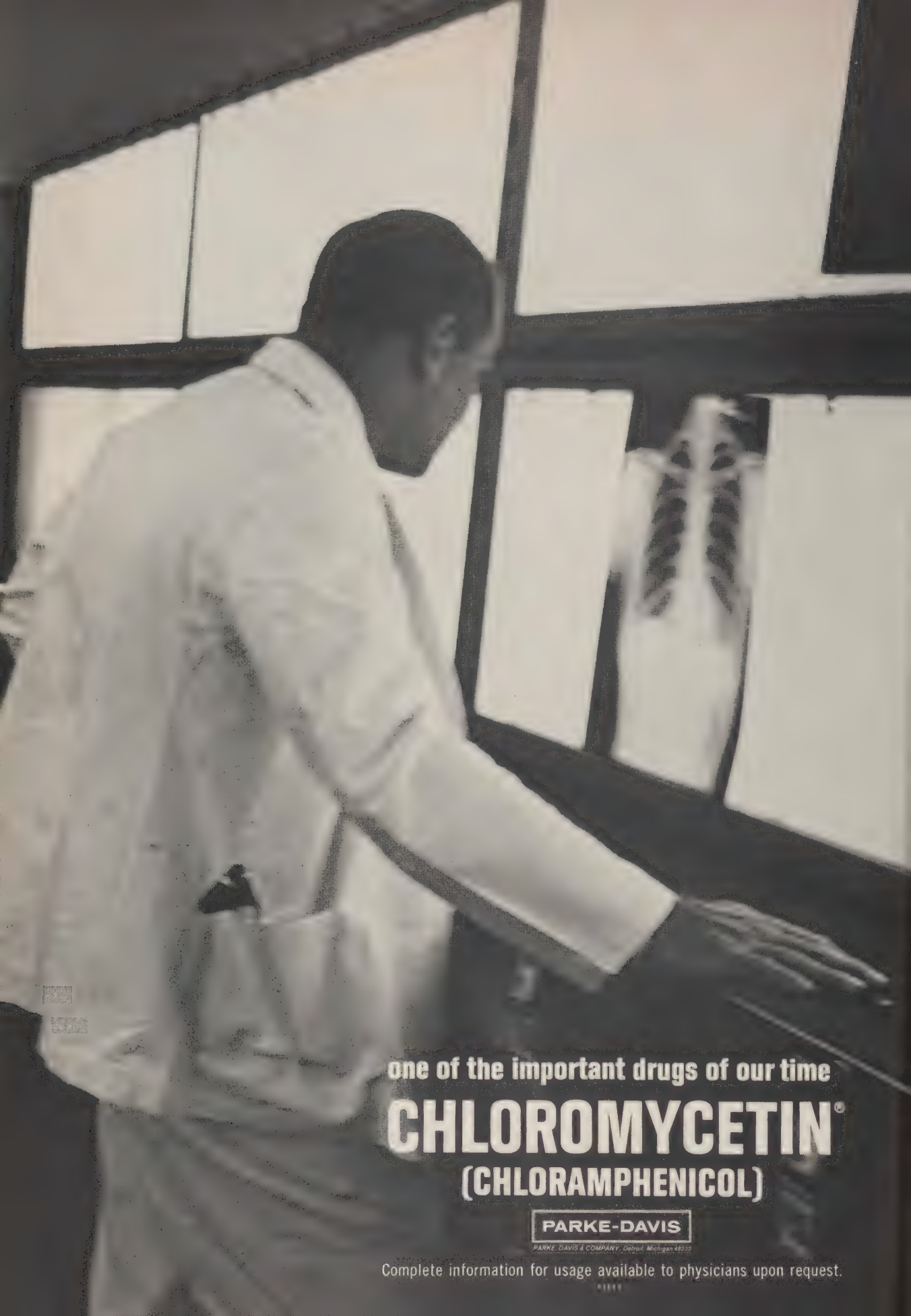
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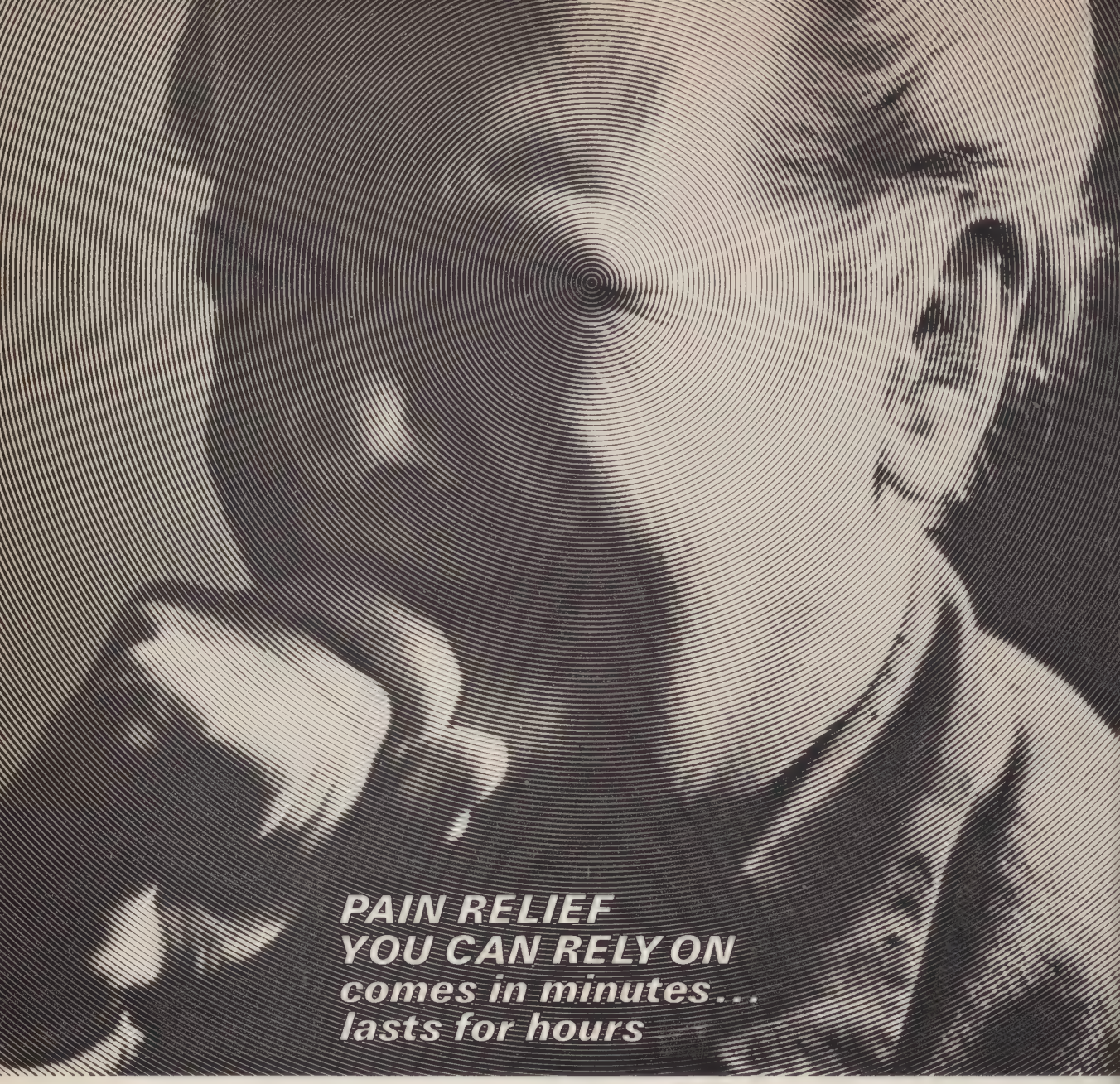
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The Psychiatry of Presidential Assassination

Part I: Jackson and Lincoln

DONALD W. HASTINGS, M.D.

Minneapolis

PREFACE

At 12:30 P.M. on November 22, 1963, while riding in an open car with Mrs. Kennedy and Governor and Mrs. John Connolly of Texas, President John F. Kennedy was struck in the back by a 6.5-mm. bullet; seconds later another shattered the right side of his skull. They were fired from a surplus Italian military rifle equipped with a 4-power scope. The trigger was pulled by Lee Harvey Oswald, age 24, father of two. The distance was from 75 to 90 yards.

A stunned nation was preparing to bury its President when a second assassin shot and killed the first. Disbelief and alarm were added to the shock of grief; to most Americans that weekend has the quality of a nightmare, its harsh reality softened by a vague wonder if it ever really happened.

But this was not the first time that the United States was shocked by such an occasion; our parents and their parents' parents were equally stunned by the assassinations of Abraham Lincoln, James Garfield, and William McKinley. Four other Presidents had attempts made on their lives. We are still too close to November 1963 to place Lee Harvey Oswald in perspective, but a start can be made by viewing him in the company of his fellow assassins, about whom much is known. Their personalities are reasonably clear when looked at with hindsight, and their illnesses seem to be diagnosable at this historical distance. It is my opinion that all of them, with the exception of Oscar Collazo and Griselio Torresola, who tried to kill President Harry S. Truman, were psychotic.

I am entirely dependent on the works of others for the data from which my psychiatric conclusions are drawn. Of the authors to whom I owe gratitude—they are listed in the bibliography—Robert J. Donovan, who wrote *The Assassins*,[1] is the one to whom I am most indebted. To the reader interested in greater detail, I suggest he start with him.

INTRODUCTION

Of the possessions of Western man, government under law is perhaps the most painfully acquired. This means that each individual senses, or should, his moral obligation to settle differences by legal process and not by brute force and violence. A resort to violence threatens the very foundations of our society and is abhorred by its members. Violence is particularly abhorrent when it is directed at the highest symbol of our political system, the President of the United States. Theodore Roosevelt, yet to feel the searing burn of the assassin's bullet, said of McKinley's murder, "It was in the most naked way an

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SUMMARY OF ACTUAL AND ATTEMPTED ASSASSINATIONS OF PRESIDENTS

President	*Assassin*	*Date*	*Outcome for President*	*Psychiatric diagnosis of assassin (D.W.H.)*	*Outcome for assassin*
Andrew Jackson	Richard Lawrence	Jan. 30, 1835	Not injured: pistols misfired	Paranoid schizophrenia	Committed as insane; died in St. Elizabeth's Hospital, June 13, 1861
Abraham Lincoln	John Wilkes Booth	Apr. 14, 1865	Death	Paranoid personality with psychotic episodes	Shot by self or by soldiers in burning barn, April 26, 1865
James A. Garfield	Charles J. Guiteau	July 2, 1881	Death	Paranoid schizophrenia	Hanged, June 30, 1882
William McKinley	Leon F. Czolgosz	Sept. 6, 1901	Death	Paranoid schizophrenia	Electrocuted, Oct. 29, 1901
Theodore Roosevelt	John N. Schrank	Oct. 14, 1912	Wounded	Paranoid schizophrenia	Committed as insane; died, Sept. 15, 1943
Franklin D. Roosevelt	Giuseppe Zangara	Feb. 15, 1933	Not injured; Anton Cermak killed	Paranoid schizophrenia	Electrocuted, March 20, 1933
Harry S. Truman	Oscar Collazo and Griselio Torresola	Nov. 1, 1950	Not injured; guard killed	"Fanatics"; not mentally ill	Torresola killed in gun battle; Collazo pardoned by H.S.T., July 24, 1952
John F. Kennedy	Lee Harvey Oswald	Nov. 22, 1963	Death	Paranoid schizophrenia	Assassinated two days later by Jack Ruby

assault not on power, not on wealth, but simply and solely upon free government, government by the common people, because it was government and because it yet stood for order as well as for liberty."[2]

The assassination of a President, or an attempted one, might be motivated by

- *A conspiracy to overthrow the government.* Thus, if an enemy proposed to attack the United States with modern weapons, the assassination of the Commander in Chief immediately before the attack might create a great advantage. The confusion that resulted might lessen quick retaliation by the Armed Forces of the United States.
- *Personal reasons.* As improbable as it seems, the possibility nevertheless exists that a President could become involved, as may other men, in matters which could lead to violence: affairs of the heart, unpaid gambling debts, and so on.
- *Mental illness.* In paranoid delusional systems, the sick person is convinced that an organization is persecuting him, and he sees evidences of the persecution wherever he looks. The organization can be anything: the United States government, the FBI, the University of Minnesota, the Catholic Church, the Masons, and the like. Whatever is felt to be the persecutor, the deluded person may try to communicate with its head, requesting that orders be issued to cease the persecution, or may take matters into his own hands and attempt to kill as a means of retribution. Every chief of a large organization is only too well acquainted with letters and telephone calls from "cranks," who are, as a rule, psychotic persons. Or the attempt to kill may result from hallucinations and other kinds of delusions. Thus, if God appears to a psychotic person and commands him to take a life—that of the President, for example—this tortured soul may attempt to do just that—and, as it appears to him, for the highest religious motive.

This article will examine the minds and motives, insofar as this is possible, of the men who have attempted to kill Presidents. Four of them killed their men (see table). There have been no known attempts to kill other than by shooting, and no woman has been directly involved. (Mrs. Mary Surratt was hanged, probably in a miscarriage of justice, for her presumed part in Lincoln's death.) With the exception of Lee Harvey Oswald, who killed President Kennedy with a rifle, all the assassins and would-be assassins have used side arms at close range.

PRESIDENT ANDREW JACKSON AND RICHARD LAWRENCE, JANUARY 30, 1835

Andrew Jackson was the first American President an assassin attempted to measure. Whether the powder was damp or poorly loaded in the two single-shot percussion pistols did not matter much, because Jackson was not hurt; both of the percussion caps fired and sounded strangely loud as they echoed under the Capitol rotunda, but neither ignited the powder beneath. The at-

tempt on Jackson's life alerted a surprised American public to the fact that a President might be an assassin's victim. Hitherto such an idea had never been entertained seriously in a freedom-loving democracy that elected the President at the will of the people. Assassination was reserved for kings and despots—that was understood—and only several generations earlier there had been much public talk of the desirability of George III's death. That an American citizen might shoot an American President, however, seemed too fanciful an idea to entertain. But Richard Lawrence tried it, and Jackson probably would have been killed if the second pistol had fired; terrified observers saw that the muzzle was actually up against Jackson's chest.

The attempt on Jackson's life and the subsequent trial of Lawrence had interesting medical and historical aspects. Francis Scott Key, an enlightened man and author, in 1814, of the lyrics to the "Star-Spangled Banner," had been district attorney for the District of Columbia since 1833, and it fell to him to prosecute Lawrence. He encouraged the defense to plead insanity, and Lawrence spent the rest of his days in mental hospitals. Subsequent prosecutors and defense attorneys of insane assassins were not always this humane.

To return to the circumstances of the assassination attempt: On January 30, 1835, there was a funeral procession for Representative Warren R. Davis of South Carolina. Behind the coffin in the line of march as it left the east portico were many dignitaries, including Andrew Jackson. Lawrence stepped out, flung aside his coat, which concealed his pistols, and at 13 feet aimed his first pistol at Jackson's heart. The cap fired but the gunpowder did not. The cap report created bedlam; while people rushed at him from all directions, he transferred the second pistol to his right hand and fired point-blank at the enraged President, who was rushing at him with cane upraised. Again, the cap fired but not the gunpowder, and the President was saved.

Lawrence was born in England, coming to America with his parents when he was about 12 years old. As a child he was healthy and well behaved but a "loner." He learned house painting and, as a hobby, landscape painting. Somewhat more than two years before the assassination attempt, family and friends began to notice an alarming change in this formerly quiet man; this date, at about age 32, marks the onset of a psychosis from which he never recovered. The symptoms of mental illness were manifested by acts of violence and threats of violence, unprovoked fits of laughing and cursing and talking to himself, and loss of interest in his work. He fancied that he was Richard III and said that he owned large estates in England, maintaining that his status was such that President Jackson was his clerk. Steamship owners, he believed, had formed a conspiracy to cheat him out of his large fortune in England. He did not have to work, he said, because the United States owed him large sums of money. In a rage at his sister's maid, who he thought was laughing at him, he threatened to shoot her. Once when his landlady asked him to pay his bill, he threatened to kill her and her husband.

Probably to keep track of the progress of his fanciful claims for money against Congress, Lawrence began to frequent the halls of the Capitol. On one occasion he accosted Vice-President Martin Van Buren and told him that unless the money were paid, he or the President would fall. All the red flags signaling an approaching tragedy were raised, but no one heeded them. Today a Lawrence would almost certainly find himself swiftly in St. Elizabeth's Hospital on making such a statement to an official.

Lawrence became increasingly angry at the President. On the way to jail after the shooting he stated that the President had killed his father and that he had been an enemy of the Lawrence family for many years. He thought Jackson was holding up his claim for money and that if he killed him, Van Buren would pay the claim. He felt that Jackson was conspiring with the Duke of Wellington to deprive him of his rights. He made the point after the shooting that he had never discussed his assassination plans with anyone, assuming that everyone knew all about them; this attitude was probably a delusion of reference based on feelings that others could read his mind.

Lawrence pleaded insanity, which was the only defense that was possible. Francis Scott Key undoubtedly could have arranged a quick trial and execution had he desired, thereby winning a victory as prosecutor; the public was seething and wanted Lawrence to die. To Key's everlasting credit, he did not hang this sick man. Instead, he urged the defense to use the precedent of the famous Hadfield case, which, thirty-five years before in England, had established that if the accused were suffering from a delusion and if the deed were the "immediate, unqualified offspring of the disease," he could be acquitted on the grounds of insanity. (Hadfield was an English veteran, wounded in the head and admittedly insane, who attempted to shoot George III in 1800.) All the doctors who examined Lawrence felt he was insane, and he was acquitted.

He spent the rest of his days in jails and hospitals. He was the seventh patient admitted to the then-new government institution for the insane, now known as St. Elizabeth's Hospital, in Washington, D.C. Dr. Winfred Overholser, until recently superintendent of St. Elizabeth's, believes that the diagnosis would now be paranoid schizophrenia. Lawrence died on June 13, 1861, "taking his place in history as the first man ever to make an armed attack on a President of the United States."[1]

PRESIDENT ABRAHAM LINCOLN AND JOHN WILKES BOOTH, APRIL 14, 1865

On a spring evening in 1865, Abraham Lincoln was assassinated while sitting in the Presidential box of Ford's Theatre in Washington, D. C. Although in 1865 the country was in flames, no American President had yet been assassinated. True, Richard Lawrence had tried his luck on Andrew Jackson thirty years before, but that was long ago and the lesson had been forgotten. The Secret Service, organized in 1865, dealt mainly with the many counterfeiters who were busy with printing presses after the Civil War. It would not be until Theodore Roosevelt took office in 1901 that the Secret Service would be directed to protect the life of the President. Garfield and McKinley would be killed before this came about. Although there had been much talk and many fears about plots to assassinate Lincoln, as late as July 15, 1862, Secretary of State William H. Seward could say, "There is no doubt that from a period anterior to the breaking out of the insurrection, plots and conspiracies for purposes of assassination have been frequently formed and organized. . . . [A plot] need furnish no grounds for anxiety. Assassination is not an American practice or habit, and one so vicious and so desperate cannot be engrafted into our political system."[3]

The life of John Wilkes Booth, because he was part of a famous family, is the most amply documented of those of the assassins. "For roughly seventy years between the arrival of Junius Brutus Booth [John Wilkes's father] from England in 1821 and the death in 1893 of Edwin, the most distinguished of his sons, the Booths were the pre-eminent family of the American stage. After their father's death, three of his sons carried on the Booth fame in the theater, and it has been a common saying that Edwin ruled the North, Junius Brutus, Jr., the West, and John Wilkes, the South."[1] The Booths possessed things other than fame, however. "Edwin Forrest, the tragedian, expressed it once in replying to a friend who, incredulous at the news from Ford's Theatre, asked him if he believed John Wilkes had shot the President. 'Certainly I do,' Forrest replied. 'All those goddamn Booths are crazy.' "[1]

Five years after his marriage in England in 1815 to Adelaide Delannoy, Junius Brutus Booth was irresistibly attracted to 18-year-old Mary Ann Holmes, who sold flowers near one of the London theaters in which he played. Carrying on a surreptitious affair with her, to escape the detection of friends, he took her to the island of Madeira. There he learned she was pregnant. On about the same day, a clipper ship pulled into harbor bound for America, and Junius and Mary took it. They finally settled on a farm near Belair, Md., 25 miles north of Baltimore. This was a remote site, well away from the prying eyes of visiting English actors. It was here that John Wilkes was born in 1838, the ninth of 10 children of this union. Junius Brutus accomplished the difficult feat of raising a large family in Maryland while keeping his English wife expecting his momentary homecoming, apparently able to convince her that all this time he was traveling on the stage. He spent the winters acting and the summers farming; he is acknowledged to have been one of the greatest actors of his time, if not of all time. He was, however, psychotic in episodic bursts. In 1824 he was seized with a "violent fit of insanity," according to a newspaper account, and stabbed at a fellow actor, saying, "I must cut somebody's throat today, and whom shall I take?"[1] In terrifyingly real duels on the stage, fellow actors might find themselves fighting for their lives against Junius' flashing sword. On one such occasion in Richmond, he dueled a startled actor off the stage, out through the wings and the back door of the theater, and down the main street, finally bringing him to bay in the corner of a hotel lobby. Once, aboard a ship bound for Annapolis, noting the medicine chest and a loaded musket, he seized the latter and forced the captain to swallow six bowls of salts at gunpoint. The fate of the captain is not recorded. In 1838, again on shipboard, he leaped into the Atlantic to search for a friend, William Conway, who had committed suicide some time previously by jumping overboard. On another occasion, he did not appear for the start of Act V of *Hamlet*. Surprised stagehands brought him down from the rafters, where he was crowing like a rooster. It is clear that John Wilkes's father had psychotic episodes, possibly manic-depressive ones. In *The Mad Booths of Maryland* Stanley Kimmel says that "he was either on the heights of jubilance or in the depths of depression, and so wavered between madness and genius that no one could be certain which would predominate."[4]

On John Wilkes's thirteenth birthday, May 10, 1851, his father and mother were married. Adelaide had at last learned of the affair, come to America, and established residence in Baltimore to obtain a divorce.

From the beginning, John Wilkes Booth was treated differently by his parents. "To Edwin and his sisters he was a troublemaker and a vexation, but to his father and mother he was an exceptional child whom they petted for his bright appearance and fiery temperament. They could not keep up with his pranks, and he was allowed to run about like a wild young colt."[4] His father died a year after the formal marriage, when John Wilkes was 14 years old. At best he had not seen much of him, because of his father's long absences on the theater circuit; his mother had overindulged him to the point where he was undisciplined, unmanageable, and intolerant of any authority but his own. He had a vicious streak; he shot dogs and cats for the sake of killing them and once shot a neighbor's pig that wandered into their yard. He was an excellent marksman. "If anyone doubted his supremacy, he silenced him by placing an empty bottle at some distance, shooting through its open neck, and blasting out the bottom without nicking it elsewhere."[4] Any attempt to correct him frustrated him so badly that he might go into a tantrum. As a student he was only average, soon got bored, and had trouble with the self-discipline that schooling required. He went to several schools but did not accomplish the equivalent of a high school education.

Without question John Wilkes had real talent for the stage, but he was poorly trained. With his older brothers on the road most of the time and his father dead, he had no one to teach him in the years he could have profited most from it. Even in his best years of acting, discerning critics saw the great talent but also realized that it had been poorly developed. He embarked on his professional stage career at age 17, capitalizing on the family name. As his debut he played Richmond in *Richard III* (as his father had done long before) in Baltimore. Two years later when he was with a stock company in Philadelphia, several bad errors and forgotten lines made him a laughingstock; he resented this deeply, a resentment that in some measure accounted for his identification with the cause of the South.

Around this time (mid-1858), a set of events occurred that were to have a marked impact on John Wilkes and, in turn, on the United States. Stung by poor reviews and unable to compete with his brother Edwin, he accepted an offer of $20 a week with a Richmond stock company. He found a far different reception below the Potomac. Blessed with a handsome face and body and a famous name, he was welcomed by the select of Southern society, adored by Southern women, lionized by rich plantation owners, hailed as a great actor, and given marvelous reviews. Not surprisingly, he accepted the Southerners as people who could understand him and whom he could understand. In adopting the South, he adopted its cause. However, although loudly espousing it, he never cared enough to fight for it. He was briefly one of the Richmond Grays, a fashionable unit of the state militia, when it was sent to guard the hanging of John Brown. (He is reported to have become faint when the old man dropped through the trap.) John Wilkes had borrowed a uniform to go with the group. This was the extent of his soldiering, although in later years he enjoyed telling of his fantasied part in John Brown's capture.

When the war came, theater in the South all but collapsed. Rather than remain in the South and share her hardships, perhaps even her combat, John Wilkes chose to return to the North he despised and to continue his stage career, which by now had become spectacular. In one year of the war he made more than $20,000, a large sum in those times. In the last winter of the war John T. Ford, owner of Ford's Theatre in Washington, paid him $500 for a one-week engagement. On November 9, 1863, President Lincoln attended Ford's Theatre to see Booth play dual roles in *The Marble Heart*. Seventeen months later the two were to find themselves together once again in Ford's Theatre, this time in the Presidential box, Booth with murder in his heart and a derringer in his hand.

Booth took all his prejudices north with him. He joined the Knights of the Golden Circle, a secret, pro-rebel society. He was so outspoken about his Southern sympathies on occasion that the management warned him to desist lest he ruin his career. "In the spring of 1863 he and an actor named T. L. Conner were arrested in St. Louis for publicly denouncing the Lincoln administration. Booth was accused of having said he 'wished the whole damned government would go to hell.' Conner was sent to prison, but Booth got off with a fine after taking the oath of allegiance to the Union."[1] Later, he attacked John Sleeper Clarke, husband of his sister Asia, and almost choked him to death, because Clarke had made a derogatory statement about Jefferson Davis, President of the Confederacy. In 1863 in Chicago he was overheard saying, "What a glorious opportunity there is for a man to immortalize himself by killing Abraham Lincoln!"[1]

Booth was a man of many temperaments, quick changing and mercurial. Particularly in the latter days of the war, he was morose and pessimistic. He drank more heavily than usual and spent many of his nights in hotel rooms with women of casual acquaintance. In one of his tirades against the President, he claimed that Lincoln had been elected through a fraudulent count of the votes. As time went on, he became obsessed with the idea that Lincoln was trying to become king of the United States.

It was perhaps about this time, in 1863 and two years before the assassination, that John Wilkes entered upon a paranoid illness which lasted, with ups and downs and aggravations by alcohol, until his death. Years after John Wilkes's death, Edwin wrote, "We regarded him as a good-hearted, harmless, though wild-brained boy, and used to laugh at his patriotic froth whenever secession was discussed. That he was insane on that one point no one who knew him well can doubt. When I told him I had voted for Lincoln's re-election, he expressed deep regret and declared his belief that Lincoln would be made King of America, and this, I believe, drove him beyond the limits of reason."[1]

Toward the end of 1863 his voice began to crack because of the severe demands of the many leading roles he was playing. At first the disorder was regarded as simple bronchitis and laryngitis that would soon disappear. It never did in full, however, and his career on the stage was essentially over. He continued to act, but his appearances became farther and farther apart.

Now, however, new dreams of glory were submerging his interest in the theater. His thoughts were turning daringly toward the leading role in a new and different kind of drama, one that offered hope of boundless fame and a chance of settling old scores with Abraham Lincoln and the North.

In April, 1864, General Grant terminated the exchange of war prisoners, on which the South depended as a source of the replenishment of its armies. With Lee's casualties and desertions increasing, the order was a desperate blow to the South, and Booth decided to take it upon himself to provide a desperate remedy.[1]

His plan, not original with him, was to kidnap the Commander in Chief and exchange him for the Southern prisoners in Northern hands. Although the sheer industrial weight of the North already had the Confederacy crushed, a transfusion of released Southern prisoners undoubtedly would have prolonged the war even if it had no chance of altering its outcome. The abduction of Lincoln had been a point of discussion on numerous occasions by the top Confederate command, but they had turned it down as unrealistic. Even in Booth's mind, the plan of abduction did not involve the death of Lincoln, only the use of him as a form of currency with which to barter for Southern prisoners. It was on this basis—help for the South but no talk of harm to Lincoln—that Booth was able to collect a crew of co-conspirators. When the plan changed from kidnapping to murder, most of them faded into the shadows. Unfortunately for them, the judicial process made no such nice distinctions after the assassination, and everyone, including the woman in whose boarding house the conspirators met, was hanged.

As difficult as the abduction plan might have appeared to Confederate leaders, 26-year-old, impulsive Booth saw no insurmountable problems and organized a motley group of men to help him. It was essentially a one-man conspiracy aided by unimportant people impressed with John Wilkes and the Booth name and to some extent motivated by the Southern cause. Among those later convicted as conspirators were David E. Herold, feebleminded and out of work; George A. Atzerodt, German-born, a coward with a fierce look, a wagon painter, and a small-time blockade runner; Lewis Paine, feebleminded or insane, son of a Baptist minister and, like Booth, swearer of allegiance to Union causes; John H. Surratt, Jr., Confederate spy and clerk of an express company in Washington; Mrs. Mary Surratt, John's mother, a widow, owner of a tavern and a rooming house, Confederate sympathizer, and hotelkeeper for blockade runners; and Dr. Samuel A. Mudd, physician and setter of John Wilkes's fractured ankle after the assassination.

The abduction conspiracy started about September of 1864 in a Baltimore hotel. Booth thought of kidnapping Lincoln as he attended a theater production and spiriting him below the Southern lines before anyone could interfere. Toward the end of 1864 he stopped in Philadelphia and deposited with his sister Asia a sealed envelope that contained a letter not known to have been read by anyone until after the assassination. In the letter he explained why he was attempting to capture the President. " 'More than any other document perhaps,' said Carl Sandburg, 'this letter gave a key to J. Wilkes Booth, his scrambled brain, his vanity and self-importance, his level of ideas and reasoning about that of an eighth-grade schoolboy, his ham actor habit of speech and phrase, his desire to show the South that he was a Confederate hero even though they no longer loved or cared about him.' "[1] The letter, given complete in *The Assassins*, is long, rambling, and incoherent.

In the first three months of 1865 Mrs. Surratt's

Washington house, only eight blocks from the White House, was used as a conspirators' den to plot, over ample drinks on numerous occasions, the capture of Lincoln but, be it noted, not his murder. Of the several plans devised for Lincoln's abduction, none was carried out.

By the latter part of March 1865 Booth was talking of murder instead of abduction, and the group of conspirators took alarm. Most vanished from the scene, not wanting the blood of a President on their hands.

On April 9, 1865, Lee surrendered to Grant at Appomattox Court House, and any purpose to kidnap the President to secure the release of Southern prisoners came to an abrupt end. Whatever Booth's previous motivations, from this point on the only purpose could be murder. He conceived an incredibly desperate plan: paralysis of the Union government by several simultaneous murders. He would assassinate Lincoln, Atzerodt would shoot or stab Vice-President Andrew Johnson, and Paine would kill Secretary of State Seward. General Grant was included later when Booth found that he would be in the theater box with Lincoln. By getting rid of these four men on one evening, Booth, in his psychotic mind, apparently thought he could strike some sort of blow for the South. Sober reflection could only have brought a sane man to the conclusion that Lincoln's death would put an end to any hope of a peaceful settlement for the South. Unfortunately, Booth was not a sane man.

George S. Bryan[3] records a number of first-hand observations that were made about John Wilkes in the several months preceding the assassination. Several are of psychiatric interest:

• "Heretofore regarded as temperate for those hard-drinking times, Booth now was consuming astonishing quantities of liquor, though possibly only one that knew him well could have discerned it. Brandy was said to be his favorite tipple. . . ."

• "Writing from Franklin, Pennsylvania, on February 21st [1865], his agent [Joseph H.] Simonds compained:

" 'Your strange note of the 16th rec'd I hardly know what to make of you this winter—so different from your usual self. Have you lost all your ambition or what is the matter.' "

• "During that fatal winter . . . there was on [John's] part what Asia called 'a turn towards the evil.' It was a drift. . . . He was becoming quick-tempered; he seemed weary and feverishly abstracted."

• Booth frequently stopped by a billiard parlor in Washington to watch one of the owners, John Deery, American billiard champion, practice or play a match. "Deery, about Booth's age, had come to know him as one who never boasted of his career, had none of the 'staginess' then frequent in his profession, kept his own counsel, and was most ingratiating in manner. It now appeared to Deery, in these earliest days of spring, that Booth was laboring under a great stress. He was drinking much more freely and at times 'seemed a bit crazed,' yet he gave no inkling of the nature of the deep turmoil within him."

• The Senate chaplain, Rev. Thomas Bowman, had his attention attracted several times by Booth, then a stranger to him, in the Capitol. "[Booth] had affected him most unfavorably and awakened in him dim suspicions. On April 10 he called to inform the President, but Lincoln smiled . . . and said he didn't think anybody would attempt his life."

• On April 11 Booth and Herold were in the crowd gathered to hear President Lincoln's comments about the Southern surrender a few days before. Upon hearing Lincoln remark that he regretted that the franchise in Louisiana had not been given to Negroes, Booth is said to have become enraged and muttered, "That means nigger citizenship. Now, by God, I'll put him through!"

• On the morning of April 13 E. A. Emerson, a member of the Ford company, was standing in front of the theater as John Booth walked up. Emerson had acted with Booth, was well acquainted with him, and said of him, "He was a kind-hearted, genial person, and no cleverer gentleman ever lived." John now was evidently in a bad temper. He grabbed a cane from Emerson's hand and said:

"Ned, did you hear what that old scoundrel did the other day?"

Emerson asked him whom he was talking about, and John flung back:

"Why, that old scoundrel, Lincoln. He went into Jeff Davis' house in Richmond, sat down and threw his long legs over the arm of a chair and squirted tobacco juice all over the place. Somebody ought to kill him." (Lincoln did not use tobacco in any form.)

"For God's sake, John," Emerson interposed, "stop where you are! I'm going to quit you."

At that, John bore down with such force on the cane, which he had been holding across his shoulders by its ends, that it snapped in four pieces.

• During the afternoon of April 13, looking in on C. D. Hess, manager of Grover's Theatre, who was busy reading a manuscript with the prompter, Booth sat down and insisted on talking. Hess thought this behavior was out of character for Booth, who usually was extremely courteous.

On April 14, Good Friday, Booth by chance dropped by the Ford Theatre to pick up his mail; by equal chance he overheard the manager re-

mark that Lincoln and Grant would attend the play that evening and that a messenger had only recently arrived from the White House to reserve the box. Lincoln had, with foreboding and reluctance, given in to the begging of his wife to attend this benefit performance. Booth realized at once that the President, as if by providence, had fallen into his murderous web. Hurriedly he made preparation during the course of the afternoon. He inspected the Presidential box, bored a hole in the door of the box with his pen knife to peek through, and jammed another door shut with a board so that no one could enter and interfere with him.

That afternoon General and Mrs. Grant backed out of the invitation, and President and Mrs. Lincoln invited young Major Rathbone and his fiancée to attend the play with them. That evening, after the curtain had risen on the first act at Ford's, Atzerodt defected on his assignment to kill the Vice-President. He was hanged anyhow. Paine almost succeeded in killing Seward by stabbing. He left five wounded men in the Seward house as he fled.

The shooting of Lincoln at point-blank range, Major Rathbone's ineffective attempt to stop Booth, the leap to the stage, the spur catching on a flag hanging in front of the box, the broken left leg, and the mad dash by horse across the Anacostia River are familiar to all Americans. Booth lived like a hunted animal for the next twelve days. He might have had a chance to get out of the country had it not been for the fractured leg.

During the chase, Booth made entries in his diary that are of psychiatric interest: "I can never repent it, though we hated to kill. Our country owed all her troubles to him, *and God simply made me the instrument of his punishment* [my italics]. . . . I bless the entire world. Have never hated or wronged anyone. This last was not a wrong, unless God deems it so, and it's with Him to damn or bless me."[1] The next day Booth and Herold, his last companion, succeeded in crossing into Virginia and were befriended by a Southern family who were probably not aware of the identity of their guests. The assassination was discussed, however, and a daughter suggested that Booth killed the President for money. Booth replied, "It is my opinion he wasn't paid a cent, but did it for notoriety's sake."[1] At about 2:00 A.M. on April 26 Union soldiers surrounded the family's barn, where Booth and Herold were sleeping. Ordered out, Herold surrendered. When Booth refused to come out, an officer set the barn on fire. In the light of the flames, soldiers saw Booth draw his revolver. A shot rang out. Booth was dragged from the barn with a bullet wound behind his right ear. It was never determined whether one of the soldiers shot him or he shot himself. The latter version is usually accepted. He died a few hours later, saying, "Tell mother I died for my country. I have done what I thought was for the best."[1]

(To be continued in April)

IN TREATMENT OF ACUTE OTITIS MEDIA in children, similar results are obtained with tetracycline, erythromycin propionate (Ilosone), a long-acting mixture of benzathine penicillin G (Bicillin), or demethylchlortetracycline (Declomycin). The preparations are superior to a mixture of sulfamethazine, sulfadiazine, and sulfamerazine (Terfonyl). Tetracycline appears to be the best choice even though 20 to 40% of strains of Streptococcus pyrogenes isolated from hospital patients resist its action. In 463 episodes of acute otitis media, all but 6 to 15% of patients were cured by seven days of therapy with tetracycline, erythromycin propionate, or demethylchlortetracycline or by single injection of a long-acting mixture of penicillin G. Failure rate was 22% after administration of a triple sulfonamide preparation.

GUNNAR B. STICKLER, M.D., and JAMES B. MC BEAN, M.D., Mayo Clinic and Foundation, Rochester, Minn. J. Amer. med. Ass. 187:85-89, 1964.

The "False-Positive" Sputum Cytology

The Problem of the Extrathoracic Primary

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THE ACCURACY of sputum cytology in the diagnosis of bronchogenic carcinoma is well established. The 3 patients to be reported below had repeatedly positive cytologies during evaluation of symptoms or X-ray findings suggesting a primary lung tumor. In each, subsequent examination showed an upper airway carcinoma in the absence of a definite lung lesion.

CASE REPORTS

Case 1. A 50-year-old man was admitted on Oct. 5, 1962, for evaluation of headache of seven months' duration. The patient reported a right frontal parietal headache that initially was easily relieved with aspirin but that became more constant and more severe over this time interval. Approximately one month before admission the patient had developed a cough productive of a whitish sputum. When seen in the medical clinic a positive sputum cytology was obtained. The patient reported no other symptoms. He had smoked 2 packs of cigarettes per day for at least thirty years. He was admitted to the hospital for further examination.

While in the hospital at least 4 more positive cytologies were reported. An extensive radiological evaluation was completed, which included routine chest films (Fig. 1), laminograms, bronchograms, and magnification views of the suspicious areas of the chest. Initially under suspicion were both perihilar areas which were shown to contain small cystic structures on bronchography. No bronchial obstruction was discovered radiologically. Bronchoscopy performed six days after admission was negative. A left scalene node dissection showed no tumor. Reexamination by bronchoscopy, including direct laryngoscopy ten days after admission, revealed

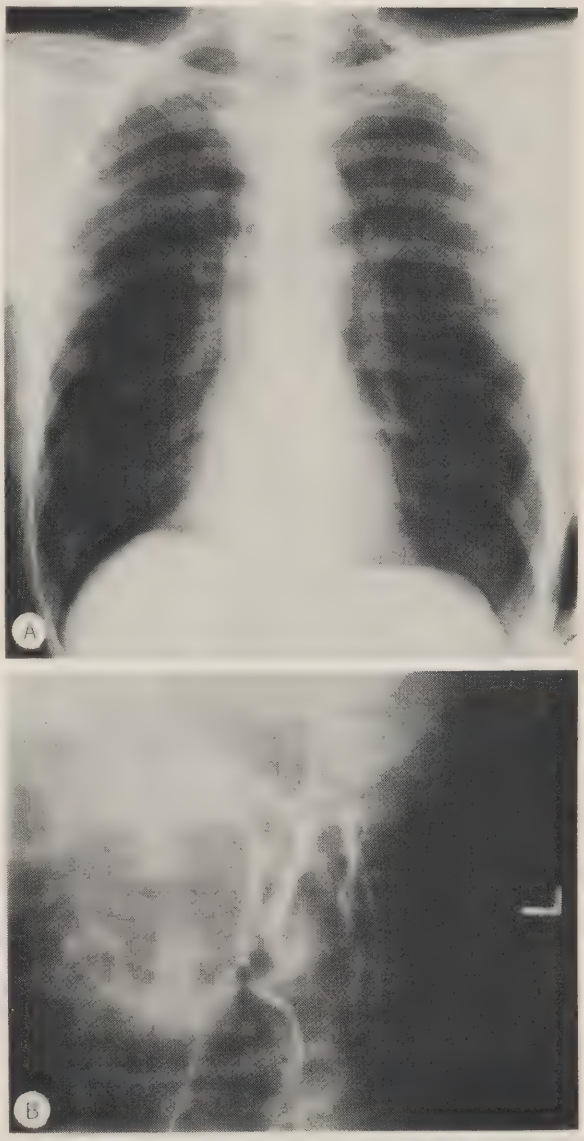


Fig. 1, Case 1. (A) Routine chest film; no primary lesion demonstrated. (B) March 1963 laryngogram demonstrating transglottic tumor on right

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Fig. 2, Case 2. (A) Chest film, after recovery from acute congestive heart failure. Residual pleural changes at right base. Prominent hilar shadows. No specific primary malignant lesion. (B) Laminogram of larynx. Supraglottic tumor on left



no tumor. It was during this time that repeat positive sputum cytologies were obtained. The patient was discharged with the presumptive diagnosis of bronchogenic carcinoma, primary site unknown.

The patient was readmitted on Feb. 23, 1963, with pain on the right side of the neck, difficulty in swallowing, and a 20-lb. weight loss. Direct examination showed a huge carcinoma of the right side of the larynx with involvement of the adjacent lymph nodes, also shown on laminograms of the larynx (Fig. 1). Treatment by tracheotomy and radiation was unsuccessful, and the patient died from progressive tumor on April 12, 1963.

Case 2. A 63-year-old male was admitted on Jan. 3, 1963, with complaints of shortness of breath, cough, and fever and was treated for congestive heart failure and pneumonia. On physical examination he was found to have a carcinoma of the prostate which was treated with orchidectomy and appropriate chemotherapy. Two samples of sputum obtained at the time of admission were positive for carcinoma. Bronchoscopy revealed no lesion. Chest X-ray after improvement from congestive heart failure and pneumonia showed no specific lesions (Fig. 2). The patient was discharged on Feb. 1, 1963.

He was readmitted Feb. 26, 1963, because of bloody sputum and a feeling of burning in the throat. He had suffered no change in his voice. On direct laryngoscopy examination, a large supraglottic carcinoma of the left side of the larynx was seen. This was also shown on laminograms (Fig. 2). The tumor was resected in a radical neck dissection, with 2 of 7 nodes being positive for tumor. The patient has been followed for one year and remains well.

Case 3. A 54-year-old man was admitted on April 29, 1963, for treatment of known active pulmonary tuberculosis. The patient was treated with isoniazid and para-aminosalicylic acid. Because the admission chest film (Fig. 3) showed nodular lesions, sputum cytologies were done. Beginning July 1, 1963, and continuing through the rest of 1963, 4 of 9 cytologies were positive, and several specifically were diagnosed as epidermoid carcinoma. During the continuing treatment for tuberculosis, examination of sites for extrapulmonary primaries was carried out, including laryngoscopy and bronchoscopy which showed no tumor. During treatment the nodular lesion in the left upper lobe resolved, and there was no significant change in the contracted right upper lobe to indicate progressing tumor (Fig. 3).

On one occasion, in July 1963, the patient had

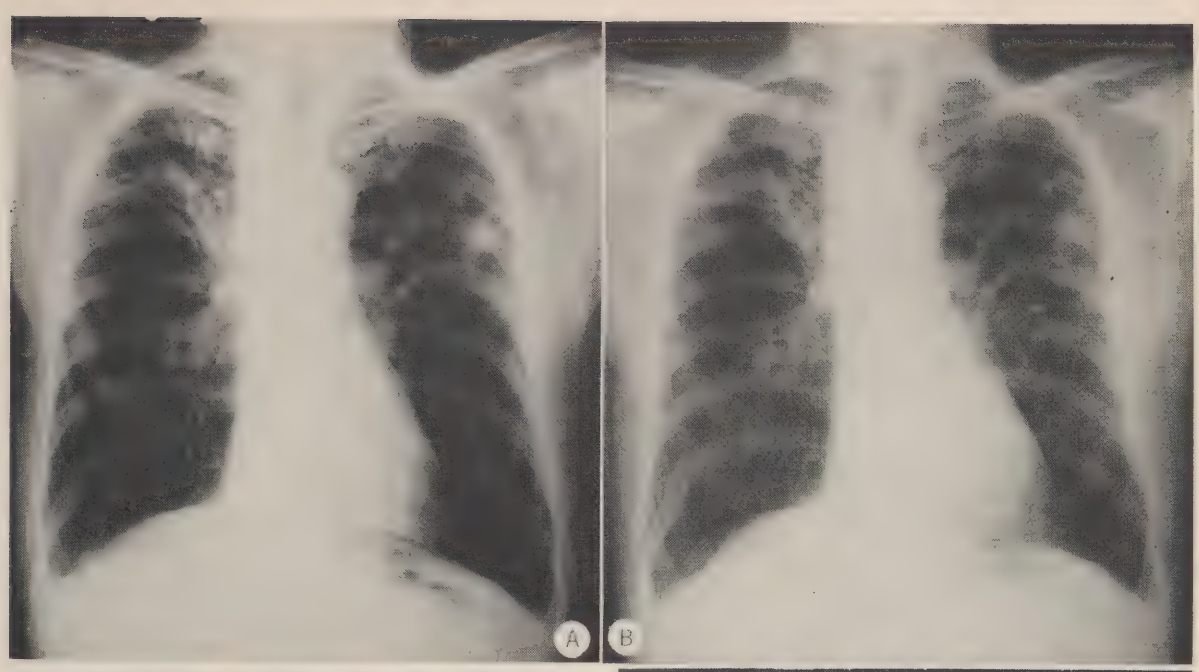




Fig. 3, Case 3. (A) July 1963 admission chest film. Fibrotic, contracted right upper lobe. Nodule over left third anterior rib. (B) Dec. 1963—little change in right upper lobe. Nodule in left upper lobe has regressed. (C) Jan. 1964—sinuses: opacification of right maxillary antrum with bony destruction

a severe nosebleed requiring packing. During the first six months of hospitalization the patient complained several times a week of a headache for which he received medication from the nurses. This was not brought to the attention of his physicians until Dec. 1963, when the patient more specifically described right facial pain rather than a true headache. Because of this, X-rays of the sinuses were ordered, showing destruction of the right maxillary antrum (Fig. 3). Biopsy showed epidermoid carcinoma; also, carcinoma in situ was found at the right choana. The patient is currently receiving radiation therapy.

DISCUSSION

In case 1, despite the fact that laryngoscopy was negative at the time of the initial admission, the possibility remains that, if the larynx were examined by laryngography at the time of the bronchography, the site of the primary tumor might have been recognized at that time. In the second case actually very little delay ensued between the report of a positive cytology and the discovery of the primary tumor. In case 3, a six-month delay might have been avoided if the patient's complaints had more carefully been evaluated and also if sinus films were included as a routine in the evaluation of a patient with a positive cytology and no definite pulmonary primary. Admittedly, in this case, the presence of active tuberculosis with the secondary abnormalities made it extremely difficult to rule out the presence of tumor within the areas of inflammatory disease. The nodular lesion in the left upper lobe was first considered the primary tumor, but this became unlikely as the lesion resolved under antituberculosis therapy. When this occurred, attention was centered on the contracted right

upper lobe as a source for a hidden primary tumor within the scar. The patient refused right upper lobectomy that was advised before the true site of the primary tumor was recognized.

The accuracy of sputum cytology in various series is high. The incidence of false-positive studies is reported to be as low as 0.2%.[1,2] The value of sputum cytology in the preoperative diagnosis of pulmonary cancer is best indicated by the work of Umiker,[3] who reports that this was the single most likely source of a positive diagnosis in these patients. He reports an incidence of 25% positive preoperative diagnosis with sputum cytology, as against 8.6% for the next most common source of diagnostic pathological specimen, that of bronchial biopsy. He also comments, however, that the small peripheral primary lesions are the most often negative and therefore the converse statement holds that invisible or barely visible peripheral primaries are the least likely to give a positive sputum cytology. In a large series, with an extensive review of the literature reported by Grunze,[4] the cause of false-positive sputum cytologies is thoroughly evaluated. The author makes the comment that other intrathoracic diseases, such as tuberculosis, bronchitis, or bronchiectasis, were the most likely causes. He also sites single instances of chronic sinusitis and polyps of the nasal mucosa as a presumed cause of positive cytology.

Our pathologists feel that, with the criteria utilized, the likelihood of a false-positive sputum cytology is minimal. Especially important is the necessity of observing groups of malignant cells rather than single cells for a final definitive diagnosis.

Therefore, when presented with a patient in whom a positive cytology is found but whose chest X-ray is negative, the physician must look for upper airway sites of carcinoma.

CONCLUSION

Three examples of patients who were thoroughly evaluated radiologically because of positive sputum cytologies, although no definite primary pulmonary lesion was seen, are reviewed. In 2 patients the primary tumor was in the larynx and in the third, in the right maxillary antrum. In view of the current accuracy of cytological examinations, the physician must be cautioned to look for a primary tumor elsewhere in the respiratory tract when the sputum cytology is positive.

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SERUM CREATINE PHOSPHOKINASE activity is a reliable indication of muscular dystrophy. The enzyme activity among patients with muscular disorders is increased only in those with progressive muscular dystrophy or dermatomyositis. Since the enzyme is not found in liver or erythrocytes, the test is reliable in patients with hepatic disease or hemolysis. Serum enzymes were studied in 200 patients with muscular disorders. Among 10 patients with progressive muscular dystrophy, serum creatine phosphokinase activity was above the normal high of 5 units in all but 1—a 47-year-old patient whose 35-year history of the disease indicated the destructive process had ceased. The increased activity also was observed in 3 other patients with acute dermatomyositis.

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J. Pediat. 63:1116-1119, 1963.

Transabdominal Amniocentesis in the Study of Rhesus Sensitization

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THE INCREASING AWARENESS of perinatal mortality and morbidity has evoked more accurate and sensitive tests for the pregnancy complicated by rhesus sensitization. Until recently the 2 main criteria by which management was determined were (1) the history of previous erythroblastosis,[1] and (2) the determination of maternal blood antibodies.[1,2] Many investigators have attested to the fact that these methods are not highly accurate.[3–12] Recently Novell and Taylor, in Miami[2] and Robertson, in Edinburgh,[11] have documented the many pitfalls in determining the degree of sensitization. Goddard states that the maternal antibody titer is a useless prognostic sign.[3] The maternal blood studies, indeed, may only correctly predict fetal affliction in 50% of such cases. Titer levels of 1:1,000, or over, usually indicate an affected infant, but, below this level, no constant relationship exists between titer and the fetal disorder. Of all Rh negative women, 5 to 10% become sensitized, and, of these, 15 to 25% of the fetuses are lost.[3,12] Obviously, if perinatal mortality and morbidity are to improve, more accurate diagnostic measures must be used.

The pioneer work of Bevis, in 1950, on the liquor amnii, has been followed by accurate spectrophotometric evaluation of amniotic fluid, popularized by Walker, Liley, Bevis, and others.[6,7,12–16] Not only has the accuracy of determination been improved manyfold, but the method of amniocentesis has lent itself to successful intrauterine transfusions,[17] with excellent fetal salvage. The exact timing when a sensitized pregnancy should be interrupted has been a boon to clinicians using spectroscopic analysis of amniotic fluid.[2,18] Accuracy is high, varying between 70 to 97%, removing much guesswork from diagnosis.[6,7,11,12,15] A prediction based on spectroscopic analysis of amniotic fluid, which is discordant with the probabilities based on other observations, is usually the correct one.[7] Biochemical analysis is apparently superfluous, and nonrewarding.[14,16]

Bevis originally attempted to correlate the urobilinogen and nonhematin iron level of amniotic fluid samples with the fetal hemoglobin, without uniform success. Elevations in these 2 compounds were, indeed, found in 8 cases of erythroblastotic stillbirths, but while the nonhematin iron level of over 40 μg. percent indicates an affected infant, lower figures may be found in severely affected fetuses.[14,19]

It may be well to note the word of caution enjoined by Dr. Eastman in his comment, in 1956, to the article by Bevis. He noted that the safety of amniocentesis is questionable and that premature labor and other "obvious dangers" may result.[20] Warnings concerning possible amniotic infection, possible invasion of the fetal bloodstream during the procedure, and possible damage to the fetus by accidental puncture have also been voiced.[18,21–23]

METHODS AND RESULTS

Since Feb. 1964, the Geisinger Medical Center has added transabdominal amniocentesis to its diagnostic armamentaria. Selections were made on the following bases: (1) a history of previous erythroblastosis, (2) the appearance of maternal Rh antibody titers, where there had previously been none, (3) the presence of antibody titers predating the present pregnancy, (4) a significant rise in antibody titers and (5) certain apparently normal pregnancies used for controls.

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TABLE 1

COMPOSITION OF AMNIOTIC FLUID

Range or mg. percent	*Bevis[14] (1952)*	*Sozanskii[16] (1960)*
Chloride	508	622.7
Sugar	27	23.4
Protein	446	0.31%
Cholesterol	8-58	
Urea	12-37	20.68
Bile pigment	0-2.5	
Icteric index	0.2-7	
Urobilinogen	1.79	
Levulose	0-11	
Iron	26 μg.	
Copper	1.4-120 μg.	

The earliest samples were taken at twenty-four weeks, the latest, at term. The method has been well documented, but certain fundamental precautions must be stated as follows: (1) there must be no abdominal wall infection, nor preexisting amnionitis, (2) the urinary bladder must be empty, (3) the fetal position must be determined by accurate palpation or X-ray, or both, (4) location of the placenta should be determined by auscultation for the point of maximum volume of the placental souffle, by radioactive iodinated serum albumin scan (RISA), or by radiography. The placenta should preferably be avoided, although aside from the theoretical danger of entering the fetal bloodstream, little harm can be done.[4,22,24] Strict asepsis must be observed, including the operator's hands, all instruments used, and the container for the specimen.

The skin is prepared with tinted tincture of benzalkonium chloride about the site chosen. This is, preferably, 2.5 cm. below the umbilicus in the midline. A skin wheal is raised with 1% procaine solution, using a small needle. A No. 20 gauge, 4-in. spinal needle is passed into the amniotic cavity and at least 10 cc. of amniotic fluid withdrawn. This is immediately transferred to a sterile, opaque container and centrifuged at 4,000 r.p.m. for ten to twenty minutes, depending upon the turbidity present. If much sediment is present, filtration may be a necessary adjunct. Definite points of resistance are encountered during amniocentesis, which are well to be aware of. They are: the skin, the rectus fascia, the uterine wall, and the amnion. The latter structure offers resistance much like that encountered when perforating the theca interna during spinal tap. The needle is withdrawn and the puncture site cleansed and covered with a small dressing. If an outpatient, the mother is instructed to remove the dressing in twenty-four hours, and to report any redness or tenderness about the puncture site. We have encountered none in 38 punctures to date.

If blood is encountered during the tap, the needle may be allowed to clear, or be advanced further until obvious amniotic fluid is recovered. Blood usually indicates that the placenta has been traversed and, therefore, to remove the needle and reposition it may result in further trauma to the placenta. Liquor amnii, collected in opaque, sterile containers, may be kept for many months if refrigerated, but the more rapidly determinations are made, the better. Optical absorption from 700 through 340 mμ is read on a Beckman DU spectroscope. The tungsten lamp has proved sufficiently accurate but an ultraviolet source is frequently helpful. The absorption curve is plotted logarithmically on a graph, and the degree of involvement noted. The height of the curve is measured between 2 parallel, horizontal lines drawn to intersect (1) the 450 mμ line and (2) the peak. The difference will determine how severely affected the infant may be. Osmolarity and fluorescence of amniotic samples have not been fruitful.[15] It may be stated that below 6 units the infant is mildly affected, or not at all. Between 8 and 12 units, the child will usually be moderately severely affected, and above 14 units a definitely severe erythroblastosis is present. Certain pitfalls may be encountered in the interpretation of these absorption curves, the most commonly encountered of which are oxyhemoglobin and grossly infected amniotic fluid. Liley fully documents these sources of error.[7]

Since large numbers of well documented cases have been reviewed, only several representative cases will be shown from our recently initiated series. The first was an unusual and interesting case complicated by a central placenta praevia.

CASE REPORT

Case 1. A 37-year-old para 4-0-0-4 was admitted for observation at twenty-two weeks ges-

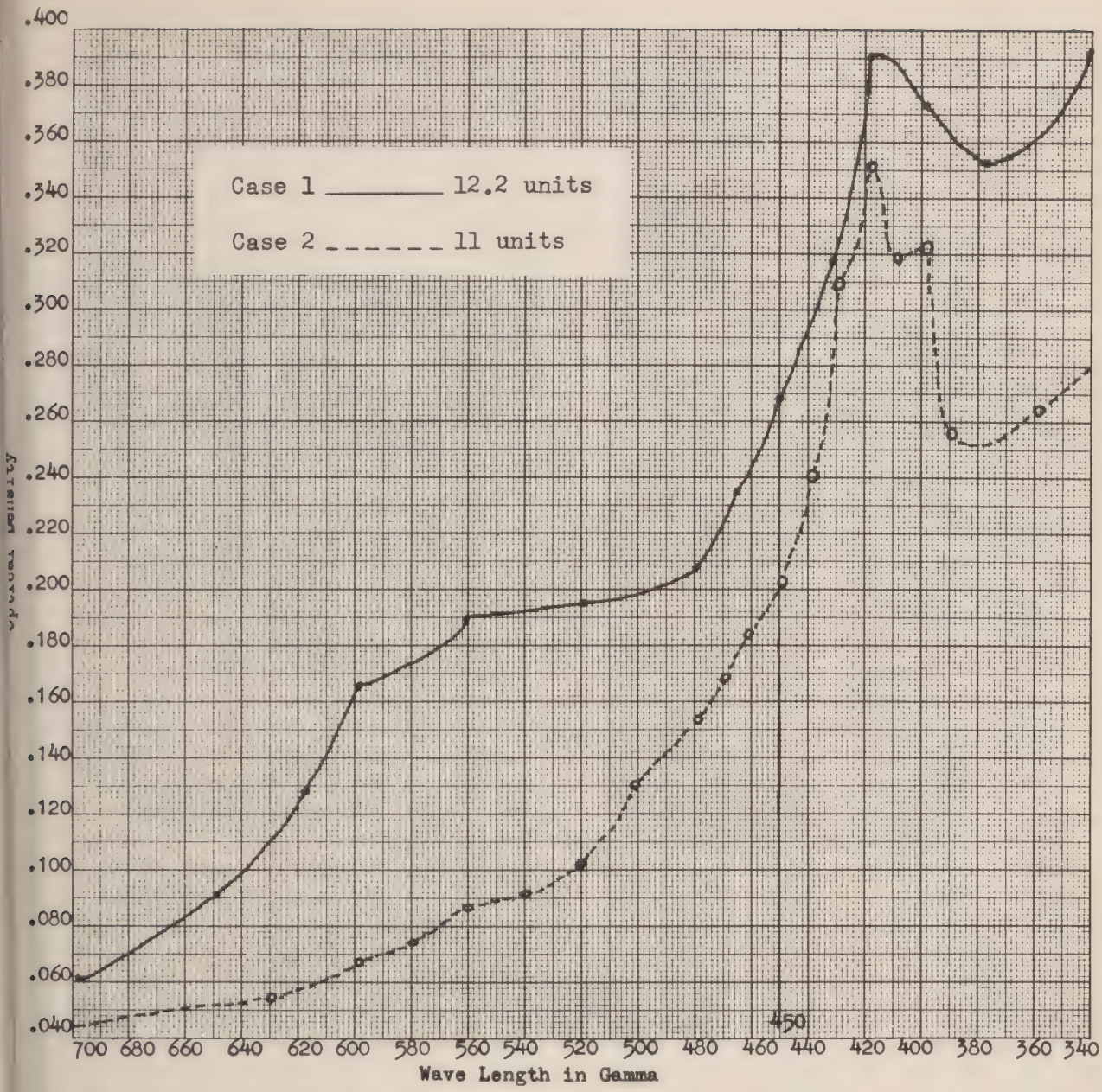
TABLE 2

COMPARISON OF OSMOLARITY OF AMNIOTIC FLUID AND BLOOD PLASMA BY DEPRESSION OF THE FREEZING POINT

Amniotic fluid in milliosmoles	*Ph*	*Blood plasma*
249 to 274(1)	7.71 to +8(1)	280 to 308(1) 320 (2)

*Data from:

1. KELLER, J. M., and WELLS, G. S.:[25] Unpublished studies on osmolarity and fluorescence of amniotic fluid.
2. CANTAROW, A., and SCHEPARTZ, B.:[26] Biochemistry. Philadelphia: W. B. Saunders Co., pp. 315, 818, 1962.



tation with a central placenta praevia diagnosed by RISA scan. Previous pregnancies showed no sensitization. At her thirtieth week, blocking antibodies appeared at 1:32. Spectroscopic examination of the amniotic fluid showed 12 units. Repeat titers at thirty-five weeks were 1:64, and repeat amniocentesis was unaltered. Delivery by cesarean section was done at the thirty-fifth week of the central placenta praevia. The infant was Coombs positive, type O, Rh positive. Bilirubin at forty-eight hours was 13.8 mg. percent. Hemoglobin was 14.0 gm. percent.

Case 2. A 29-year-old para 3-0-0-3 had blocking antibodies appearing at her thirty-fourth week of 1:2, by her thirty-seventh week 1:32, and by her fortieth week 1:64. Amniocentesis demonstrated marked involvement. A female infant, Coombs positive, type O, Rh positive was delivered. Hemoglobin was 18.5 gm. percent dropping to 10 gm. percent by forty-eight hours. Bilirubin was 2 mg. percent.

Case 3. A 31-year-old para 4-0-0-4 had no previous sensitization. At her thirty-second week blocking antibodies appeared 1:2. By the thirty-fifth week they were 1:32, and at her last prenatal visit, in her fortieth week, they reached an astounding 1:1024. Amnocentesis was done at term to demonstrate typical involvement. In-

duction by surgical amniotomy yielded a living male infant, Coombs positive, type A, Rh positive. Clinical jaundice developed thirty minutes after delivery. Hemoglobin was 13.7 gm. percent, and total bilirubin was 8.43 mg. percent. Exchange transfusion was done.

SUMMARY AND CONCLUSIONS

A brief review of transabdominal amniocentesis with spectroscopic examination of the liquor amnii has been presented. The criteria for its use, the hazards of the procedure, and the great increase in diagnostic accuracy in the prediction of erythroblastosis fetalis have been enumerated. In the absence of an adequate hospital spectroscope, properly refrigerated, sterile samples of amniotic fluid may be mailed in opaque containers to any cooperating laboratory equipped with a proper spectrophotometer.

A plea is made for the wider, but not the indiscriminate, use of spectroscopic analysis of amniotic fluid, in the continued effort to better existing perinatal mortality and morbidity due to erythroblastosis.

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Cavernous Sinus Thrombosis

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CAVERNOUS SINUS THROMBOSIS has never been a common disease. However, the frequency declined when the use of sulfonamide and antibiotic medications eradicated most infections that formerly would have progressed to cavernous sinus thrombosis. Consequently, reports of series of cases with almost 100% mortality have been replaced by reports of single cases with almost universal recovery.

This is a report of an acute, fulminating, septic cavernous sinus thrombosis with bacteremia due to a coagulase-positive staphylococcus. The patient, a young student nurse, survived and had minimal residual disability.

CASE REPORT

On Feb. 16, 1960, a 19-year-old student nurse was admitted to the Deaconess Hospital, Grand Forks, North Dakota, with pain in the right eye and swelling of the right eyelids of two days' duration. During the preceding two weeks she had had coryza, persistent obstruction of the right nasal cavity, and, finally, a sanguinopurulent exudate from the right side of the nose. Four days before admission there was slight aching in the right cheek. The following day, a dentist found no cause for the pain. Dental roentgenograms were negative. Two days before admission the lids of the right eye swelled, and there was pain in the right orbit. Therapy with penicillin and demethylchlortetracycline orally was begun. The swelling of the lids of the right eye gradually increased and extended to include the right side of the face. There was considerable pain in and around the right eye. On the morning of the day of admission the lids of the left eye began to swell. There was associated fever and lethargy. Penicillin was administered intramuscularly.

The family history, past history (except for nonparalytic poliomyelitis in 1946), and review of systems were negative. There were no episodes of significant nasal or paranasal sinus infections in the past.

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Physical examination revealed an alert, young woman lying in bed with her eyes closed. Temperature was 103.6° F. (orally). Pulse was 120 a minute and blood pressure, 120/70 mm. Hg. There was considerable edema of the lids of both eyes, more so on the right. The right side of the face, mostly around the eye but also involving the nose, was swollen. There was proptosis, marked on the right and slight on the left. There was chemosis of the right eye. A red, granular, palpebral conjunctiva bulged above the free margin of the right lower eyelid. The 2 right eyelids could scarcely be separated. Active or passive separation of the left eyelids enabled one to see 80% of the left iris. The functions of the extraocular muscles of the right eye were quite restricted, but those of the left eye were not limited. Funduscopic examination of the left eye was negative. There was a mucopurulent exudate in the right nasal cavity. The neck was not stiff, but motions of the head aggravated the pains in the head. There was no Kernig's sign or unequal or abnormal reflexes. The remainder of the physical examination was negative.

Immediate therapy was instituted intravenously with aqueous penicillin G, 1 million units; chloramphenicol, 1 gm.; and heparin sodium, 100 mg., and orally with warfarin sodium, 35 mg. The aqueous penicillin G was repeated four times and the chloramphenicol, three times intravenously, at eight-hour intervals. Heparin sodium, 100 mg. intravenously every four hours for 5 doses (controlled by Lee-White clotting times), was administered. Subsequently, prolongation of the prothrombin time was excessive as a result of the initial dose of warfarin sodium. Vitamin K_1, 10 mg., was given orally on Feb. 19, when the prothrombin time was one hundred sixty-one seconds (control sixteen seconds). Subsequently, the prothrombin time was maintained at 1½ to 2 times the control value, with daily oral doses of 2.5 or 5 mg. of warfarin sodium.

Feb. 17. The patient had a shaking chill. There was no further swelling of the eyelids or face, but the neck was somewhat stiff. The movements

of the globe of the left eye were rather limited. A program of procaine penicillin G, 1 million units intramuscularly every five hours, and chloramphenicol, 250 mg. orally every four hours, was begun.

Feb. 18. The edema of the lids of the left eye was minimal, and the extraocular movements of the same eye were not limited. The neck was stiff. The patient was alert and cheerful. Cultures of the purulent exudate in the right nasal cavity and of the blood had been obtained on Feb. 16. A coagulase-positive staphylococcus that was resistant to penicillin and streptomycin was obtained from both cultures. Penicillin was stopped; oral triacetyloleandomycin, 500 mg. initially and then 250 mg. every four hours, was begun.

Feb. 19. There had been no diminution in the swelling of the right eyelids or of the right side of the face. The palpebral conjunctiva of the right lower lid still herniated through the palpebral fissure. The left optic disk was flat, but there was blurring of its superior and inferior margins.

Feb. 20. The right upper eyelid was less tender and swollen, and the right palpebral fissure could be widened enough to expose the lower portion of the cornea. The right side of the face was less swollen, and the neck was no longer stiff. Hemoglobin was 11 gm. percent, and the leukocyte count was 11,300 per cubic millimeter.

Feb. 21. Both chloramphenicol and triacetyloleandomycin were reduced to 250 mg. orally every six hours. Roentgenograms of the paranasal sinuses revealed a markedly dense right maxillary sinus and haziness of the ethmoid air cells; no bone destruction was evident.

Feb. 22. The right side of the face was less swollen. This was the last febrile day—the oral temperature rose to 100° F. at 3 P.M.

Feb. 23. The right upper eyelid was slightly ecchymotic, there was less proptosis, and there was limitation of upward gaze with the right eye. The granular, red, palpebral conjunctiva still protruded above the right lower lid. Temporally there was pallor of the right optic disk. The superior and inferior margins of both optic disks were blurred. Both pupils were round, regular, and equal and reacted to light, directly and consensually, and to convergence. Hemoglobin was 12.3 gm. percent, and the leukocyte count was 8,000 per cubic millimeter.

Feb. 24. There was slight tenderness over the right maxillary sinus.

Feb. 25. The patient was able to breathe through the right side of the nose for the first time since the onset of this illness. The patient was dismissed to the home of the admitting physician and given chloramphenicol and triacetyloleandomycin, 250 mg. of each orally, every six hours for the succeeding five days and a daily dose of warfarin sodium, 2.5 mg. orally, for three days. The patient promptly returned to the University of Minnesota and earned a B.S. degree in nursing.



Fig. 1. Cavernous sinus thrombosis, Feb. 17, 1960, with bilateral edema of eyelids and bilateral proptosis



Fig. 2. Cavernous sinus thrombosis, Feb. 21, 1960, with subsidence on left and lessening on right of edema of eyelids and proptosis



Fig. 3. Cavernous sinus thrombosis, Jan. 1964, with minimal residual edema of right upper and lower eyelids

On Dec. 21, 1962, the upper and lower lids of the right eye were still just perceptibly edematous, and the right optic disk was quite pale. There was considerable constriction of the visual field, especially of the inferotemporal quadrant, for the right eye. No other residual effects of the 1960 bilateral cavernous sinus thrombosis could be detected.

DISCUSSION

Cavernous sinus thrombosis was first observed at necropsy by Duncan in 1821, and the first clinical report was made by Bright in 1831, according to most authors.[1,2] However, Lyons[3] was able to unearth clinical and necropsy descriptions of the disease made by Dease in 1778.

The cavernous sinus is situated at the side of the body of the sphenoid bone. It extends from the superior orbital fissure to the tip of the petrous portion of the temporal bone, a distance of slightly more than 2 cm. The sphenoid sinus lies medially, and the middle cranial fossa with the temporal lobe lies lateral to it, while the hypophysis lies medial to and above it. The sinus is made up of many compartments that become fewer as age advances. It contains the carotid artery and the sixth nerve that lies lateral to the artery. The third, fourth, and ophthalmic (sometimes the mandibular as well) divisions of the fifth nerve lie in its lateral wall, in that order, from above, downward. Anteriorly it receives the sphenoparietal sinus; the superior ophthalmic vein, which in turn receives the anterior and posterior ethmoid veins and veins from the frontal diploe; and the inferior ophthalmic vein that drains the outer portion of the floor of the orbit. The inferior ophthalmic vein communicates with the facial veins and with the veins of the pterygoid plexus. The middle cerebral vein and veins from the hypophysis and from the sphenoid sinus empty directly into the cavernous sinus. Through communications with the precentral and postcentral veins that empty into the superior longitudinal sinus, the middle cerebral vein establishes communication between the superior longitudinal and the cavernous sinus. Through emissary veins the cavernous sinus communicates with the pterygoid plexus and by the carotid plexus with the internal jugular vein. Posteriorly, it gives off the superior and inferior petrosal sinuses. The superior petrosal sinus runs in the attached margin of the tentorium cerebelli above the trigeminal nerve and empties into the lateral sinus. The inferior petrosal sinus, shorter but larger than the superior, passes with the sixth nerve below the petrosphenoid ligament and enters the internal jugular vein. Each cavernous sinus communicates with its fellow of the opposite side through the anterior and posterior intercavernous sinuses.

Courville[4] reported the finding of septic thrombosis of the cavernous sinus in 50 of a series of 40,000 autopsies. The various causes of the lesion were listed as facial furuncles or cellulitis (15 cases), otitis media (8 cases), ethmoidal and sphenoidal sinusitis (8 cases), dental infection (2 cases), and tonsillitis (2 cases) and 1 case each of nasal ulceration, erysipelas, puerperal sepsis, ophthalmitis, carcinoma of the cheek, gunshot wound of the frontal region, accessory nasal sinus disease, and subdural abscess. In 7 instances the exact cause was uncertain because 2 or more possible factors were present.

The 3 most common causes of thrombosis of the cavernous sinus are marasmus, trauma, and infection.[1,2] Marasmic thrombosis usually occurs in association with debilitating conditions at the extremes of life. Any injury to the skull may cause thrombosis of the cavernous sinus; usually there is an associated fracture of the base of the skull. Septic thrombosis is by far the most common form of cavernous sinus thrombosis and is nearly always secondary to a thrombophlebitis of one of the afferent or efferent veins. However, it may also be due to direct extension from basilar meningitis, abscess of the postorbital space, suppurative sphenoiditis, or suppuration of the petrous portion of the temporal bone. The bacteria most often reported are Staphylococcus aureus, Staphylococcus albus, Streptococcus pyogenes, and pneumococcus.

Thrombosis of the cavernous sinus has been divided according to the virulence of the course[2,5] into the acute fulminating type or the chronic compensatory type but in general is categorized into the anterior and posterior varieties.[6,7] Spread of infection from the face or mouth is by the anterior route by way of the facial vein through the angular vein and the superior ophthalmic vein and, from the ear or mastoid, the posterior route through the afferent veins of the cavernous sinus itself. The anterior variety represents the more acute and fulminating infections, with direct involvement of the cavernous sinus in the septic process.[8,9] The posterior variety usually is due to retrograde propagation of a thrombus via the dural venous sinuses into the cavernous sinus.

Many cases reported as cavernous sinus thrombosis have not been accepted as such. Orbital cellulitis, sphenoidal sinusitis, and so on[8] can present a similar clinical picture. Eagleton[5] in 1926 listed criteria that most authors accept as necessary for justifying a clinical diagnosis of

cavernous sinus thrombosis. The criteria are exophthalmos, chemosis, edema of the eyelids, partial to complete paralysis of the ocular muscles, progression of signs from one eye to the other, a source of infection, and generalized sepsis.

The exophthalmos, chemosis, and edema of the eyelids are due to the orbital congestion due to thrombotic obstruction of the ophthalmic vein[10] as it enters the cavernous sinus. Walsh[9] attributes these signs mainly to infection in the orbit rather than to venous obstruction. The paralysis of the ocular muscles is due to involvement of the third, fourth, and sixth cranial nerves as they pass through or in the wall of the sinus. Progression of signs from one eye to the other is the result of propagation of the thrombus and spread of infection through the anterior or posterior intercavernous sinus to the contralateral cavernous sinus. Headache does not usually occur unless there is meningeal irritation from perisinus infiltration or suppuration of bone in the vicinity of the meninges.[5]

Although Chisolm[1] in 1920 reported the case of a 12-year-old boy who had a cavernous sinus thrombosis as well as a subsequent Staphylococcus aureus septicemia with metastatic abscesses and recovered on symptomatic therapy (except for stock and autogenous Staphylococcus aureus vaccine), the mortality rate for cavernous sinus thrombosis has been quite high. Review of the literature provided a figure of nearly 100% in 1936.[2] "The acute fulminating type of cavernous sinus infection holds out the least hope of response to any form of therapy" was written by Cavenagh[11] also in 1936. Cavenagh cited 7 recoveries: 3 by direct surgical approach on the cavernous sinus and 4 by generalized bloodstream therapy. Yarington[12] in 1961 reported a mortality of 80% in 878 cases in the literature.

The advent of the sulfonamides was the turning point in the treatment of cavernous sinus thrombosis. MacNeal and Cavallo[13] were the first to report a successful outcome. They treated a 40-year-old woman who had a cavernous sinus thrombosis and bacteremia due to a hemolytic streptococcus with sulfanilamide, antistreptococcus serum, and a specific bacteriophage. Other authors[14,15] reported recoveries with the use of sulfonamides alone.

Florey[16] was the first to use penicillin in the treatment of cavernous sinus thrombosis. Subsequently, numerous reports of recovery from acute fulminating cavernous sinus thrombosis have appeared.[7,16] Penicillin and the other antibiotics[6,7,17–20] have been utilized.

Lyons[21] in 1941 introduced the use of heparin into the regimen of therapy of cavernous sinus thrombosis. The rationale of anticoagulant administration is to prevent (1) further thrombosis of the venous sinuses and thus prevent further interference with the venous drainage of the brain and (2) dissemination of septic emboli with the formation of widespread miliary abscesses. The coumarin derivatives have also been utilized[18] for anticoagulation. Yarington[12] was unable to find any statistical support to justify the use of anticoagulant therapy in this disease.

Walsh[9] found necrosis in the hypophysis in 5 of 6 patients who died from cavernous sinus thrombosis. This necrosis was due to infarction. Walsh postulated that pituitary insufficiency may be the cause of prostration, systemic collapse, and death in some patients with this disease. Brown[6] advocates careful clinical observation for signs of hypopituitarism to clarify this problem.

Solomon, Moses, and Volk[19] administered prednisone orally, apparently for its anti-inflammatory effect. There was rather prompt improvement in the patient's "grave ocular situation" following the institution of steroid therapy on the thirty-seventh day of hospitalization. There was no evidence of adrenal insufficiency in their case.

Pratt[18] suggested the use of buccal streptokinase-streptodornase (Varidase®). This enzyme may (1) control the edema of the eyelids and (2) facilitate entry of antibiotics into septic areas. The efficacy of this medication has not been demonstrated.

The case reported here represents an acute, fulminating, bilateral cavernous sinus thrombosis and bacteremia due to a coagulase-positive staphylococcus. The response to antibiotic and anticoagulant therapy was quite prompt and resulted in eradication of the infection. Most likely, without anticoagulant administration, the effect of the antibiotic drugs would not have been so rapid, and there would have been more prominent residual effects of venous obstruction due to the thrombosis.

SUMMARY

1. Cavernous sinus thrombosis does not occur frequently.

2. Infection is the commonest cause of cavernous sinus thrombosis.

3. Thrombosis of the cavernous sinus occurs via the anterior or posterior routes.

4. Infection is usually responsible for thrombosis of the cavernous sinus, via the anterior

route, and retrograde propagation of a thrombus, via the posterior route.

5. The course of infection via the anterior route is usually acute and fulminating and via the posterior route, chronic and compensatory.

6. The prognosis for cavernous sinus thrombosis is no longer hopeless, due to the development of the sulfonamide and antibiotic drugs.

7. Present-day therapy of cavernous sinus thrombosis depends mainly on the antibiotic preparations and anticoagulant drugs.

8. Further attention needs to be directed toward the occurrence and detection of pituitary necrosis and insufficiency due to cavernous sinus thrombosis; perhaps the judicious use of adrenocorticosteroid drugs will further improve the survival rate for this disease.

9. A case of acute fulminating cavernous sinus thrombosis has been presented; the causative organism was a coagulase-positive staphylococcus; and the outcome of therapy with antibiotic and anticoagulant drugs was prompt and quite successful.

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HIGH ARTERIAL PRESSURE apparently activates a feedback mechanism in the healthy rat kidney that has an antihypertensive effect. The mechanism is checked by low normal pressure. When blood from a rat with renal hypertension is circulated at full pressure through an isolated healthy kidney, the animal's blood pressure falls. When the normal kidney is perfused at a low normal pressure, however, blood pressure in the hypertensive animal remains constant. Isolated kidneys were perfused at high pressure with blood from 11 rats with average blood pressures of 200 mm. Hg, while perfusion pressures of 85 to 95 mm. Hg were used in experiments with another 13 animals whose pressures averaged 208 mm. Hg. After an hour and a half of perfusion the average reduction in blood pressure was 40% greater in the first group than in the second. The difference was 26% after two hours.

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Why Is This Nail Abnormal?

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DISORDERS OF THE NAILS are both fascinating and confusing. Changes in nail shape or color are easily seen, but the causes are often poorly understood. Consequently, much folklore has developed regarding nail dystrophies. A review of nail anatomy and growth provides an explanation for some of these abnormalities.

Nail development. The skin is composed of 2 major layers, the inner dermis and outer epidermis. The cells of the epidermis progress outward and become flattened to form keratin, the outer sheath of the skin. During the third fetal month, the sheet of epidermis which covers the dorsum of each distal phalanx is invaginated to form a transverse nail groove.[1] The proximal portions of both the upper and lower surfaces of the invagination then continue forming keratin, but this keratin is of a specialized "hard" nature. The formative portion of the nail groove includes the proximal part of the posterior nail fold and the nail bed out as far as the lunula (Fig. 1). Very little keratinization occurs beyond this point. The limiting walls of the posterior and lateral nail folds mold these keratinizing cells into a flat plate which can only expand toward the end of the digit.[2] Thereafter, the new keratin which is formed at the proximal portion of the nail pushes the previously formed nail plate distally, where it slides over the nail bed to the end of the digit.

The rate of nail growth fluctuates from month to month, with a trend toward decreasing growth rate with increasing age.[3] Fingernails grow at the rate of 0.1 to 0.15 mm. per day and are completely replaced in three to four months. Toenails grow more slowly, taking at least six months for replacement.

Keratinization defects. Systemic illness may be reflected by impaired keratinization of the skin and its appendages, the hair and nails. Acute illnesses such as myocardial infarction, a bout of ulcerative colitis, or pneumonia can produce transverse white lines, ridges, or even a complete transverse break in all 20 nail plates (Fig. 2). As the patient improves, normal nail keratinization is restored and the deformed area of the plate is pushed outward and eventually lost.[4]

Transient inflammatory disorders involving one or a few fingers or toes will produce transverse lines or ridges only in the associated nails (Fig. 3). If the abnormality is persistent, prolonged formation of abnormal keratin will produce a linear dystrophy of the nail (Fig. 4).[4]

Traumatic defects. External pressures can damage a normal nail after it has emerged from the posterior nail fold. It is often possible to determine by inspection whether a nail dystrophy stems from abnormal keratinization or is due to some external factor. As shown in figure 1, the proximal edge of the nail plate runs straight across the finger. Dystrophies due to disturbed keratin formation appear as straight or slightly convex lines across the nail plate. Nail defects produced by trauma usually take the shape of the forces of pressure. The prime example of this is the series of concave white lines paralleling the posterior nail fold which are produced by the weekly manicure (Fig. 5). Another example is that due to the practice of spreading hairpins by forcing the tip of the thumb between the prongs of the hairpin. The repeated pressure of the pin on the center of the thumb nail causes V-shaped waves and ridges in the distal half of the nail.

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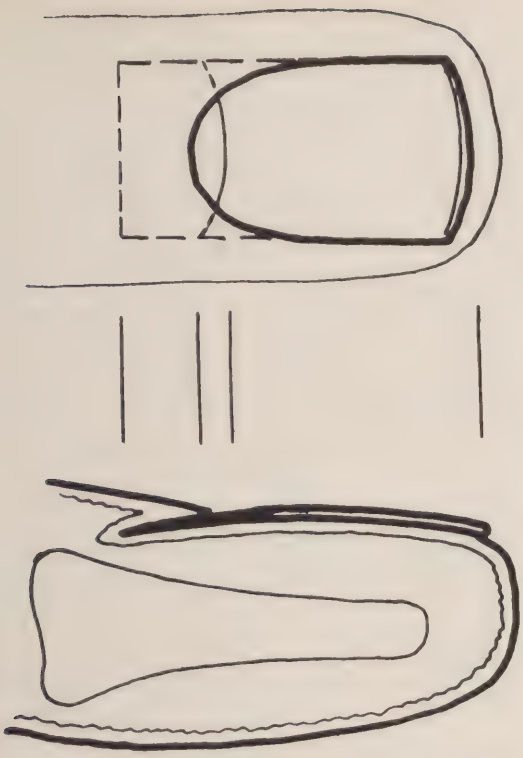


Fig. 1. Dorsal and saggital views of nail. Note continuity of epidermis around nail base.

Horizontal splitting of the fingernails, often attributed to brittleness, is a frustrating problem for both patient and physician. Free nail edges chip off in layers so that it is impossible to manicure the nails to an oval or point. This splitting tendency has been attributed to hyper- or hypofunction of the thyroid glands, disturbances in calcium and phosphorus metabolism, and vitamin deficiencies. I am not aware of studies which have established clinical or laboratory evidence for such systemic disturbances, and therapeutic programs employing desiccated thyroid, calcium, or vitamins have not been consistently beneficial.

The ingestion of one 7-gm. packet of gelatin daily for three to four months has been reported to be associated with the development of firm nails.[5] It has been suggested that gelatin supplies amino acids to form either the nail keratin or a "cement substance" which holds the keratin lamellae together. As Kligman has indicated,[6] gelatin is hydrolyzed into its constituent amino acids during digestion, so theoretically any protein should be effective in supplying the needed nutrition. In practice, gelatin is often tried but is frequently disappointing.

An important clue to the problem of splitting nails may be that this condition is seen almost exclusively in women, primarily those engaged in housekeeping and family care. The fingernails of these women are exposed repeatedly to soapy water, wet diapers, household cleansers and solvents, oils, nail polish remover, and trauma from all sorts of dry materials. Furthermore, the defect occurs at the free edge of the fingernail, which suggests external causes rather than growth deficiencies. The toenails are seldom involved, which is also evidence against a systemic defect. Many women volunteer the information that when they are away from their household chores for two or more weeks the nails lose their brittleness. This is too short an interval for growth changes to reach the distal nail, but it is long enough for the brittle, chipped nail edges to be replaced by relatively untraumatized nail. In summary, the external actions of trauma and various solvents may play a major role in the formation of brittle nails, and protecting the nails from these may be the simplest and most effective therapy.

Onycholysis, or the separation of the distal nail plate from the nail bed, is another common prob-

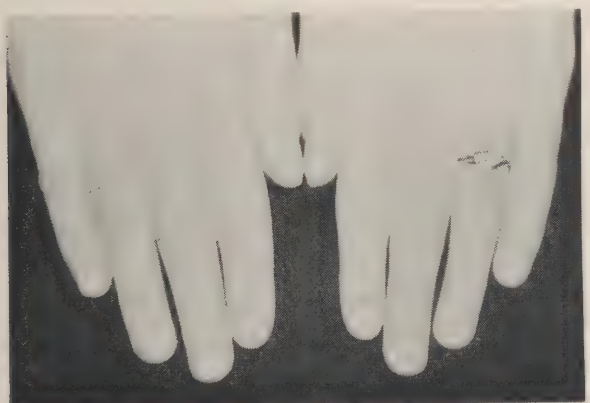


Fig. 2. Transverse white lines in all nails two and a half months after exacerbation of ulcerative colitis



Fig. 3. Transverse grooves in first and third toenails following dermatitis of those digits. Second toe not involved

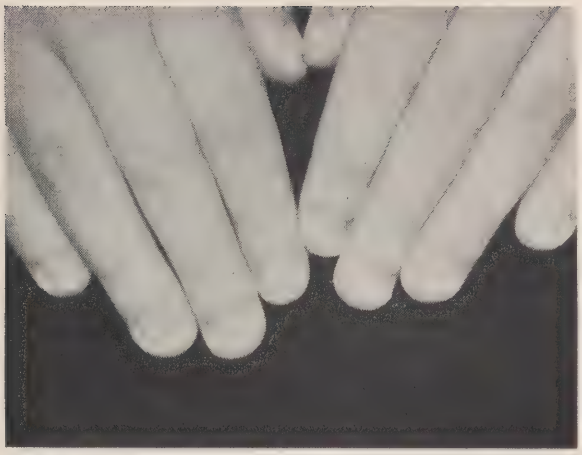


Fig. 4. Linear nail dystrophy due to chronic impairment of keratinization in patient with ectodermal defect



Fig. 5. Concave white lines due to weekly manicure



Fig. 6. Fungus infection starts at free edge of nail and moves proximally.

lem. It develops in hyperthyroidism with diffuse goiter,[7] in which case it usually appears first on the ring fingers and disappears when the thyrotoxicosis is treated. It is not a constant or specific sign, however, since it has also been attributed to hypothyroidism, syphilis, and arthritis. It is seen in fur workers and those doing wet work (trauma and solvents?), and it has appeared as a manifestation of phototoxicity due to demethylchlortetracycline. It is usually self-limited if the underlying factors are controlled.

Fungus infections. In explaining nail disorders to the patient, the lowly fungus is frequently the scapegoat. Although fungi commonly infect nails, they are often falsely accused. One may avoid this error along with the misuse of costly therapy if it is recalled that the fungi infect the nail at its distal margin and then grow proximally in splinter-like projections, gradually destroying the ventral and then the dorsal part of the nail plate (Fig. 6). Therefore, a nail dystrophy which appears first at the proximal nail fold cannot be due to fungus. An office test which often helps establish the diagnosis of onychomycosis is the potassium hydroxide mount. A small sample of the keratotic debris from the nail is placed upon a microscope slide with a few drops of 10 to 20% potassium hydroxide. After warming the slide over an alcohol lamp to hasten digestion of the keratin, the material is examined microscopically for the presence of branching hyphae.

SUMMARY

Selected disorders of fingernails and toenails have been discussed, with an attempt to relate their development to disturbances in nail keratinization. Some abnormalities are produced by preceding systemic illnesses, local inflammation, or local trauma to the digits, all of which can interrupt normal keratinization.

Splitting at the free edge of the fingernail is a common problem among housewives. The most important point in management may be protection of the nails from solvents and trauma.

Fungi do infect nails but they are often falsely accused of producing nail dystrophy. A potassium hydroxide mount helps establish the diagnosis of fungus infection.

Excerpts from a talk presented to Heart of the Lakes District, Minnesota Academy of General Practice, May 28, 1964, at Detroit Lakes.

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Role of the Nurse in Tuberculosis Eradication

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ALTHOUGH in recorded history numerous reports indicate that care was given phthisical (consumptive) persons many centuries B.C., the first organized attempt to control with ultimate eradication as the goal probably belongs to Sir Robert Philip of Edinburgh, Scotland. In 1887 he established the first well-organized clinic for tuberculosis patients in the world. He was a careful observer and initiated long-range follow-up studies on persons with this disease in its various stages. Thus, he established fundamental facts about tuberculosis that have since been of great value to tuberculosis workers around the world.[1]

"Glancing back to 1850 we find nursing for the most part a despised domestic service in relatively few secular hospitals of that period; and it should be noted that neither then, nor at any previous time, did nursing have any real connection with medicine."[2]

"In 1900 the services of 'trained nurses' were usually available only to patients in general and in very few mental hospitals, to the well-to-do, and in the larger cities to the poor in their homes. Rural folk were almost wholly dependent on friendly neighbors or persons described as 'experienced' or 'practical' nurses."[3]

With the appearance of the American Journal of Nursing in October 1900 an important educational medium was provided for nurses everywhere and, henceforth, nurses became most effective and helpful, not only in care of the sick but also in the promotion of all good health activities. They have played a dominant role in the marked increase in the span of human life in this country.

My work with student nurses began in the fall of 1914 when assigned to teach a first-year class. From 1920 to 1960 a course in tuberculosis was given annually to student nurses in 1 municipal and 4 private hospital schools of nursing. From 1923 to 1957 a course on tuberculosis for public health nurses was given throughout 3 separate quarters per year in a school of public health.

Beginning in 1927 in the hospital schools of nursing the tuberculin test was administered to all students on admission and to the nonreactors every six months as long as they were in school. Roentgenograms of the chests of those who reacted to this test on admission and those who subsequently became reactors were also studied. For those who developed clinical tuberculosis, treatment was administered or recommended.

My clinical and epidemiologic work with public health nurses, including school nurses, began in the spring of 1921 when a special school and clinic was opened for children with tuberculosis in state and municipal permanent tuberculosis clinics and in clinics organized by county public health nurses in many rural communities. Thus, numerous opportunities were afforded to observe the tuberculosis situation among students and graduate nurses themselves and also to see the great magnitude of work done by them.

Nurses indispensable in tuberculosis control program. Early in this century, the nursing profession was recognized as an indispensable ally in the management of the tuberculosis problem. Large numbers of people were then sick with this disease, and probably the majority of adults were infected with tubercle bacilli. Every nurse, regardless of her interests and major activities, was confronted with tuberculosis. Despite their small number, the nurses did magnificent work. As they increased in number, their activities extended into the various fields where they were so needed. As the years passed, the nursing pro-

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fession exerted a tremendous influence in the fight against tuberculosis among people of all ages of life.

They were at work in the prenatal clinics, in the obstetricians' and general practitioners' offices instructing expectant mothers and their families concerning the possibility of tuberculosis in their own bodies and how to prevent their newborn infants from becoming infected. Nurses were taking an active part in the families with preschool children, including the summer roundup. They were in the schools of both urban and rural communities giving instruction and service from the kindergarten through the senior high school years. They went into the colleges and universities with a special interest in tuberculosis as a part of the health program among students and personnel. As young adults entered upon their life's activities, there were the nurses going into the factories and every place where sizable numbers of people were working. They went from farm home to farm home; in fact, everywhere they were transmitting information concerning health. As people grew old, there were the nurses informing them about the prevalence of communicable tuberculosis in their period of life and how to control it.

When individuals developed evidence of ill health and went to the offices of their physicians or to clinics, there were the nurses assisting and arranging for every necessity. When persons were sent to hospitals and sanatoriums, they immediately met the nurses who conducted them to their rooms and wards and did everything possible to relieve suffering and to restore them to good health. When surgery was indicated, it was the nurse who consoled and encouraged, followed them to the operating rooms, participated in the operations, accompanied them back to their rooms, and hovered over them, keeping close watch for the slightest evidence of impending danger. All the time they were developing and maintaining morale, thus allaying fear and worry of the patients and the members of their families. Too often the importance of the services of the nurse has not received deserved recognition. For example, when drastic surgical procedures have been performed, such as thoracoplasty or pulmonary resection, nearly all of the credit has gone to the physicians who made the diagnoses and those who did the operations, while sight was almost lost of the nurses who so carefully prepared the patients psychologically for the operations, who so ably assisted the surgeons with the operations, who provided understanding nursing care in the institutions, and who participated in developing satisfactory follow-up care for the patients upon discharge. Sight also has often been lost of the importance of the anesthetists, frequently nurses, who had the very lives of patients in their hands throughout the operations.

When tuberculosis patients left the hospital or sanatorium, nurses often accompanied them to their homes and cared for them through dangerous periods. In less severe cases, public health nurses called at the homes periodically to assist, instruct, and make sure that adequate care was provided.

In times of war, nurses have served their country loyally and admirably. Wherever our military forces were established at home or abroad, there were our nurses, and not infrequently they were participating in tuberculosis work. Following wars, they engaged in caring for veterans with tuberculosis in hospitals.

Nurses suffered serious health hazards. For much of this work nurses paid a terrible price. Indeed, this price was paid by many students in schools of nursing. The Relief Fund Committee of the American Nurse Association made a report[4] in June 1930 which revealed that, of 543 nurses who had received aid since 1911, 258 (47.5%) had tuberculosis. A paper was presented before the National Organization of Public Health Nursing at the biennial convention, Milwaukee, in 1930, calling attention to this fact, in which it was said, "One of the greatest problems in the field of tuberculosis at the present time is the control of the disease among one of the most valuable groups of workers in the entire campaign—that of the nurses."[5] This statement was based not only upon the personal observations of the author but also upon reports of several other observers during the previous few years.

Numerous opinions were voiced regarding the reasons for so many students of nursing becoming infected with tubercle bacilli and developing clinical tuberculosis, such as overwork, particularly the menial kind often assigned to students, and overcrowded living quarters with poor ventilation. In the minds of many persons, age seemed to be the main factor, as students entered schools of nursing while they were "too young," and, therefore, only older girls should be admitted to such schools. It was asserted that all nurses became infected with tubercle bacilli; therefore, it was preferable to infect them as students while they were under the observation of hospital professional staffs. A sizable group of persons maintained that it was an asset for a nurse to have tuberculous infection because it immunized her against clinical disease. Students

who manifested fear of contact with tuberculous patients were told that the true spirit of nursing should impel them to take any risk that presented itself without fear or complaint.

Health hazard overcome. Over a period of approximately a decade before the 1930 meeting of the National Organization of Public Health Nursing, we had observed the terrible onslaught of tuberculosis among students and graduates of nursing and medicine. We had listened to the above-mentioned theories and personal opinions being offered to explain the situation. In fact, the head of one school of nursing in which tuberculosis had been especially destructive among the students announced that she had learned how to solve the problem. She gleefully explained that instead of assigning students to a three-month tuberculosis service in the junior year she had shifted that service to as near the end of their senior year as possible. To her this seemed a wonderful accomplishment, but our follow-up work revealed that the only difference was that the destructiveness began to appear a year later than in former classes, that is, the first year after they had begun practicing their profession.

In this school of nursing as many as 19% of some classes developed demonstrable lesions as students or soon after graduation. The situation was so serious that the students in the class of 1929 who were to have the tuberculosis service in 1928 learned of the serious tuberculosis problems which developed among members of the senior classes. Concerning this, a student of the 1929 class later wrote, "We did not like what we heard. Some of our best nurses had contracted tuberculosis and were very ill. The time was getting closer for our class to start the three-month period of nursing at the Thomas Hospital (tuberculosis service) and we were frightened. We had a class meeting and made up a petition. We would not go to Thomas Hospital unless we all received (1) tuberculin tests, (2) X-rays of chests before and after the three-month period of nursing, (3) fluoroscopic inspection of the chest before and after, (4) complete isolation techniques (gowns, masks, gloves, and so on), (5) sawdust for sputum cups so they could be burned, and (6) plenty of lysol and green soap. When the hospital superintendent received the petition he assured us it would be taken care of immediately and it was taken up with the board. When our class was ready for the Thomas Hospital service our requisites were ready too. Our practical nursing instructress, Miss Sylvia Melby, R.N., really drilled contagion and isolation into us." The author wishes to express great praise for the splendid work of Miss Melby, not only for providing the best available training but also in arranging for every possible protective measure against tuberculosis for student nurses.

Thus, this class of student nurses will always deserve credit for demanding that the hospital administration provide protection against tubercle bacilli of patients. Following this innovation the tuberculosis infection attack rate among student nurses declined precipitously until some classes were graduated without a single student who entered uninfected becoming infected with tubercle bacilli while in training.[6] Moreover, clinical cases of tuberculosis rapidly decreased.

In May 1932 Miss Elisabeth Phillips was employed at the University of Minnesota Hospital. She had just completed studies at the Johns Hopkins Hospital School of Nursing, where a great deal of attention had been paid to communicable disease techniques. Her first service at the University of Minnesota was with tuberculosis patients, mostly with advanced communicable pulmonary disease. For the most part, these patients had been referred from sanatoriums that did not have surgical services for such procedures as extrapleural thoracoplasty. One day while making rounds Miss Phillips suggested that an effort be made to develop communicable disease technique on the tuberculosis service comparable to that employed so effectively with other diseases. To have a nurse make such a suggestion and to express willingness to develop it for tuberculous patients inspired hope for a not-too-distant day when students and graduates of nursing would be adequately protected against tubercle bacilli.

Miss Phillips proceeded and developed an effective technique.[7] This accomplishment, together with that at Fairview Hospital, constituted the beginning of a new era, indeed, a safe era, for students of nursing and has since contributed mightily to the general tuberculosis control program in this country. There are nurses in this audience today who would have succumbed to tuberculosis during training or after graduation had it not been for the development of satisfactory communicable disease techniques.

The extensive work and publications of Badger and Spink and Badger's subsequent reports[10–12] have contributed immensely to knowledge of tuberculosis among nurses. His paper in the James J. Waring series brings the reader to date on this subject.

Phenomenal control accomplishments. When the 20th century opened, tuberculosis was classified as the first cause of death in the United States. The annual mortality rate closely approached 200 per 100,000 population. Numerous

opinions, theories, and speculations of the past were extant. None was founded on documented evidence, and none was of any avail. Some excellent information and fine armamentaria were available, but the citizenry had little awareness of them. The National Association for the Study and Prevention of Tuberculosis (later National Tuberculosis Association) was organized in 1904 for the purpose of disseminating information concerning tuberculosis everywhere among our citizenry. This was soon followed by state, regional, and county organizations so people in every nook and cranny of the country were provided with information as fast as it became available. In due time personal opinions, speculations, and theories were replaced by facts and, thus, sound methods of tuberculosis control were adopted. When the public was informed that tuberculosis was a communicable disease it was logical to prevent persons with this condition from spreading it to others. Thus, construction of sanatoriums progressed rapidly until large numbers of patients were isolated for treatment in these institutions. When the public learned that tuberculosis in cattle is transmissible to human beings, it vigorously promoted the program of health officers and veterinarians by destroying tubercle bacilli in dairy products through pasteurization or the flash method and later eradication of tubercle bacilli from cattle. These programs had little influence on clinical tuberculosis among people and animals already infected. However, they protected children against tubercle bacilli at an ever-increasing rate throughout the years, with corresponding reductions in morbidity and mortality that now extend into the fourth decade of life. Indeed in the United States the mortality rate among children under 1 year dropped from 311.6 in 1900 to 0.5 per 100,000 in 1961. The mortality rate among children from 1 to 4 years decreased from 101.8 in 1900 to less than 1 per 100,000 in 1961. Among children from 5 to 14 years the decrease was from 36.2 in 1900 to 0.37 per 100,00 in 1961. Among young adults, ages 15 to 24 years, the mortality rate was 205.7 in 1900 and 0.3 in 1961. The lion's share of the work responsible for these accomplishments was done before antituberculosis drugs and pulmonary resection became available.[13] Epidemiology, conducted largely by nurses, played an extremely important role in the decrease in infection, morbidity, and mortality rates.

Eradication is our goal. While our control measures have been excellent, eradication must be the ultimate goal. However, this goal is so far away that much more time and effort will be required to reach it than has been spent in all the past to attain our present tuberculosis status. We still have from 20 to 25% of our population harboring tubercle bacilli, and each is a potential case of reactivation or new clinical disease. Approximately 55,000 persons are reported annually for the first time to have clinical disease, with more than 75% with advanced disease on first report. The number of deaths from tuberculosis still closely approaches 10,000 annually.

Although the road leading to eradication is clear and the goal is in sight, it will not be traveled without a renaissance. Complacency resulting in decrease and even halting of effort now so generally observed can cause loss of all that has been gained this century. The nursing profession can play a large role in bringing about an awakening of our citizenry to the present frightening situation. To prompt such a revival, our citizenry must be reinformed about the importance of proceeding to eradication and the necessary steps for its accomplishments.

Tuberculin test is the master key. The phrase "eradication of tuberculosis" means annihilation of the tubercle bacillus. Obviously, this is impossible unless all tubercle bacilli can be located. Only the tuberculin test is capable of identifying people and animals with these organisms. Therefore, this test is the first and most essential part of the eradication program. It has been referred to as the "master key" for several reasons: First, within three to seven weeks after tubercle bacilli initially invade the human body the tissues have become sensitized to their protein.[14] Tuberculin contains tuberculoprotein and, therefore, whenever it comes in contact with the deeper layers of the skin of a person sensitized to it a reaction results. There is no way to detect the presence of tubercle bacilli in the human body until a reaction occurs on testing with tuberculin. Therefore, it is possible to make a diagnosis of tuberculosis by this test long before any phase of examination, including roentgenogram, is useful.

Second, since tuberculosis is a communicable disease it is obvious that a person who has become a reactor to tuberculin has been infected by someone who has the disease in the communicable stage. Usually, children do not have chronic communicable pulmonary tuberculosis; therefore, one needs to look only to those associates 12 years or older. The individual who has been tested periodically without reaction occurring and who then becomes a reactor is said to be a tuberculin convertor. This indicates that there has been direct or indirect contact with a person with communicable disease since the last test. If the interval between test administrations is sufficiently short, obviously the exposure is

recent. Therefore, a search for the responsible person is more likely to be successful than one for an individual who reacts to tuberculin on the first test or when too long an interval exists between tests. Tuberculin is harmless when properly administered; therefore, there is no danger in giving frequent periodic tests for those who have not reacted previously. Moreover, there is no danger of frequent testing with tuberculin causing the tissues to become sensitized.

Third, the success of a tuberculosis eradication program in a community is best measured by the tuberculin reaction. Testing done in any segment of the population, especially children, determines accurately the number harboring tubercle bacilli. Obviously, for each one there has existed a person with communicable disease responsible for the infection in the reactor. Testing in the same area five years later determines whether more or fewer children of the same age as those initially tested react to the test. This determines whether more or fewer communicable cases have existed during the five-year interval. Nothing but the tuberculin test provides this information.

The tuberculin test can determine legal responsibility. This is particularly applicable to student and graduate nurses. In many places tuberculosis has become a compensable disease, particularly among those working in hospitals. If a student nurse enters as a nonreactor to tuberculin and periodic retesting reveals that she becomes a reactor, the question immediately arises as to where and from whom the infection with tubercle bacilli was acquired. If it is found that, in the hospital where she works, there is a patient with communicable tuberculosis with whom she had contact, it is usually assumed that is where she acquired tubercle bacilli. If she later develops clinical disease, such as pleurisy with effusion or clinical pulmonary lesions, the responsibility lies with the person and the place of the initial infection. In many places the statute of limitations does not extend beyond six years. Therefore, if no clinical disease develops within that time the liability has expired. This is unfortunate in the case of a disease such as syphilis or tuberculosis, in which the chronic clinical forms usually result from infections of long standing, often for many years or decades. An invasion with tubercle bacilli that results in tuberculin conversion may ultimately become the basis for compensation, since it results in mental anguish and necessity of periodic examinations for the remainder of the infected person's life. Since the tuberculin reaction may now be the determining factor with reference to compensation within the period of the statute of limitations, the importance of each student or graduate nurse being examined periodically is obvious.

In addition to learning who is harboring tubercle bacilli and finding the persons responsible for their infection, the tuberculin test has a tremendous educational value, not only for school children but also for the entire school personnel and, indeed, the entire community. Just the announcement that tuberculin testing is to be done in a school arouses the interest of the entire population of the area. In rural areas and, indeed, in cities the tuberculin test has a fine reputation because it is generally known that it is through this test that dairy products that formerly incapacitated and killed so many people are made safe. It is also known that it has become a rarity in this country for a person to become infected with the bovine type of tubercle bacilli. For example, in the state of Indiana, periodic tuberculin testing of the cattle reveals only 4 to 8 reactors for every 10,000 tested.

Therefore, the public welcomes the news that tuberculin testing is being done for the children and personnel of the schools. They know that tuberculosis in people is no different from that in cattle, from the standpoint of communicability and destructiveness. Therefore, what the tuberculin test has done for the 100 million cattle of this country, it is capable of doing for 190 million people. When the testing starts in a school, it is an important day in the community. In some places numbers of parents come to the school that day to watch the testing of their children and others. More are likely to appear the day of reading of the tests. This can be made a significant day of education if it is pointed out that those children who do not react to tuberculin are not harboring tubercle bacilli but they should be retested periodically to make sure that status is maintained. On the other hand, for the few children who present reactions, one has the opportunity of informing them and their parents that they have been in contact with adult persons who have communicable tuberculosis. From these persons tubercle bacilli have reached bodies of the tuberculin reactors and there is the possibility that sometime, usually remotely, they may also have communicable tuberculosis. The occasion provides the opportunity of informing them that methods are now available that if employed meticulously are capable of preventing them from having tuberculosis. In addition to all of this information given parents and children, authentic items may be prepared for local newspapers so the entire public is abreast of the tuberculosis situation in the schools and what is necessary to improve it. At this point school

nurses can call attention to protection of preschool children against infections with tubercle bacilli so that few and ultimately none of those entering school will have been infected.

The world will always be deeply indebted to Dr. Walter L. Rathbun as superintendent and medical director of the Newton Memorial Hospital at Cassadaga, Chautaugua County, New York, for initiating tuberculin testing by nurses. In 1930 he arranged for public health nurses working in his sanatorium district to administer tuberculin tests. Although nurses are not licensed to administer and interpret such tests, Dr. Rathbun strongly approved their work under his supervision. Their work was so excellent that on his recommendation the next year the commissioner of health of the city of Minneapolis arranged for public health nurses to administer tuberculin tests in the clinics and homes and wherever they were indicated. It was observed that nurses administer and read tests with great care and accuracy. Since that beginning for which Rathbun must always be given credit, an ever-increasing amount of tuberculin testing has been done by nurses.

Important fundamental facts about tuberculosis. Long-term observations on large groups of children who reacted to the tuberculin test, now followed into the fourth and fifth decades of life, and experimental work have brought to light facts that can be used to great advantage in the tuberculosis eradication program. Tuberculosis begins to develop during the first hour after tubercle bacilli invade the body. The lesions are then microscopic and are located in various organs of the body, usually more in the lungs than any other organ. Our present diagnostic armamentarium contains nothing that detects the location or even their presence at that time. However, within the next three to seven weeks, the tuberculin test betrays them. Thus, the initial diagnosis is made purely by the tuberculin reaction. A fact of great significance is that these lesions are tuberculous as surely as the later gross lesions that result in incapacity and death. The only difference is the evolution through which the disease has passed. Therefore, when one is first able to identify persons who have minute areas of disease by the tuberculin reaction, the individual has tuberculosis and should be managed accordingly. In the majority of persons in whom these microscopic lesions develop, no incapacitating disease appears throughout the remainder of life. However, in a minority, endogenous reinfections occur that may result in acute or chronic progressive tuberculosis. This minority is sufficiently large to cause all of the incapacity and death from tuberculosis throughout the world and more incapacity and death in the world each year than results from all other communicable diseases combined.

High concentration of tuberculosis among elderly people. When tubercle bacilli invade the human body at any age of life there is apparently a strong likelihood that their progeny will remain viable and virulent for the remainder of that person's life. Inasmuch as we still have no way of destroying tubercle bacilli in the human body, our only recourse is to find by the tuberculin test all persons who are harboring them and keep them under close surveillance. With this statement the importance of protecting children from invasions of tubercle bacilli is obvious. It simply means that those who, because of neglect, acquire infections must be kept under surveillance for the rest of their lives in order that those destined to develop clinical lesions be prevented from suffering from incapacity or even losing their lives and from harming their associates.

It has been said that tuberculosis has shifted from people in early life to the elderly. However, there is no doubt that the chronic clinical form has always been more prevalent in the older people of the world. Attacks on the disease during the past few years have so reduced it among persons in the first few decades of life that the disease in the elderly, previously little noticed, now stands in bold relief.

Many of the older people of today were infected with tubercle bacilli early in life when little or nothing was done to protect them against the bovine type in dairy products or the human type from persons with communicable disease. They became ill in large numbers, and many died from decade to decade. Many of the survivors, now the old people, are still becoming ill and dying from infections they acquired in infancy and childhood. In 1962 about a 65% morbidity and a 95% mortality from tuberculosis occurred among persons of 45 years and older. The magnitude of this problem is realized when one considers that in this country in 1960 there were 52.2 million persons of 45 years and up, of whom 15.7 million were 65 years and older. An important part of this problem is to prevent the elderly infected persons from developing communicable chronic pulmonary tuberculosis and transmitting bacilli to the younger people. This problem can be solved with the tuberculin test by identifying all elderly individuals who are harboring tubercle bacilli. Immediate examinations of these tuberculin reactors will discover those who already have clinical disease, and periodic examinations of the remainder will re-

veal lesions destined to develop so early that they can be prevented from becoming communicable. Thus, their tubercle bacilli will remain corralled as long as the patients live.

Certification of schools. In the late 1930s the Committee on Tuberculosis of the American School Health Association was giving prolonged and careful consideration to the development of a method that would be most useful in freeing our school children, and personnel alike, from tuberculosis. This committee consisted of approximately a dozen physicians residing in various parts of the United States who were devoting their lives to methods of solving the tuberculosis problem. Their combined past work in this field constituted three hundred years. These physicians were experienced in all phases of tuberculosis control work, from the individual with tuberculosis to the problems of the community, state, and nation. After considering numerous possibilities they concluded that the best would be a method whereby individual and systems of schools could be officially certified on the basis of tuberculosis control work in progress. In order to test such a project they chose a state in which the workers were willing to make the initial demonstration with reference to its feasibility. The committee then appointed 3 physicians to constitute that state's subcommittee. A published report[15] in 1954 described the workings of the project. The report closed with the following: "Certification of schools has aroused so much interest and has so increased activity in tuberculosis control that we now recommend it as an excellent project for schools everywhere." Qualifications were established for certification which consisted of testing at least 95% of the school children with tuberculin. A 5% leeway was permitted to provide for those who objected on religious grounds and for those absent on the day of testing. The requirement for testing of personnel, including teachers, janitors, bus drivers, and, in fact, everyone who has contact with children, was rigidly set at 100% because it was known that more communicable clinical tuberculosis develops in adults than in children. Roentgenographic inspection of the chest was required of high school students and members of personnel who reacted to the tuberculin test. Those who had shadow-casting lesions suggesting clinical tuberculosis were promptly examined to determine the etiology of the disease. When it was found to be progressive tuberculosis the individuals were to be treated and not returned to school until the recommendation was made by the institutional or private physicians who administered the treatment.

For children who reacted to tuberculin a careful search was to be made among their adult associates for the sources of their infections. Thus, it was anticipated that the entire community would become interested in the tuberculosis project in the schools.

In this demonstration state the hope of the Committee on Tuberculosis of the American School Health Association was realized. The project became popular from the start, and in October 1945 the first system of schools received official certificates. It was found so useful in the tuberculosis eradication movement that it has since been in continuous operation, ever increasing in intensity and extent. More than 5,500 certificates have been awarded schools, and numerous remaining schools are rapidly qualifying for certification. This project proved so successful that it has been adopted by other states where it has been continuously employed.[16]

Certificates have been signed by the president and executive secretary of the American School Health Association, the executive secretary or managing director of the State Tuberculosis and Health Association, and the chairman of the State Sub-Committee of the Committee on Tuberculosis of the American School Health Association. More recently, certificates have also been signed by state health officials.

The certification of schools project is an exceedingly valuable educational medium. One of the reasons it succeeds so well is that it stimulates and promotes local pride. When one school acquires a certificate other schools in the vicinity take pride in the same accomplishment. Moreover, when a school is awarded a certificate local pride compels that it be kept valid by repeating all the qualifications of the project every two years. Another reason for its success is its completeness. It leaves no loophole such as exists when only children of a few grades are included or when no incentive is offered for total response of children and personnel.

When operated meticulously the certification of schools project spells the doom of the student or the personnel member in any category from unknowingly developing communicable tuberculosis and disseminating tubercle bacilli to others. Thus, it prevents outbreaks, of which so many are reported from year to year, consisting of a student or a member of personnel such as a teacher or bus driver spreading infection to other members of personnel and children.[17,18] Through school certification such cases can be found before they become communicable or before they have existed long enough to result in widespread dissemination. Thus, the certification project con-

verts the schools into safe places for children and personnel alike. Moreover, it sets an example for the entire community. On a number of occasions in places where certification of schools is in vogue, citizens have inquired why the project should not be extended to the entire community, and in some places this has occurred.

The Committee on Tuberculosis of the American School Health Association strongly recommends the certification of schools project to every state, and its goal is a certificate on the wall of every school, public, private, and parochial, in America.

Now practicing poor economy. A serious deterrent in the eradication program continues to be that the condition is not considered as tuberculosis until lesions large enough to cast X-ray shadows or to cause illness are present. This is a practice of bad economy because expensive procedures including hospitalization and rehabilitation are usually necessary, to say nothing of the tubercle bacilli that the patient has disseminated among associates before the diagnosis is made. It is this method that causes tuberculosis to continue to cost this nation approximately $750 million annually. Nearly all of this excessive cost can be abolished. When tuberculosis is recognized as such as soon as its presence is determined by the tuberculin test and proper steps are taken there is little or no need for hospitalization or rehabilitation. The communicable chronic form of pulmonary tuberculosis usually appears in persons with long-standing infections. When this form of the disease begins to evolve it usually does not cause symptoms until it has attained an advanced stage. This is the main reason that of the 55,000 new cases of tuberculosis reported in the United States in 1962 approximately 80% were in an advanced stage of the disease.

Most economical method. If these victims of the disease had learned while they were in school that all persons who react to the tuberculin test should be examined at least annually very few would have had the disease progress so far before it was found. When the chronic destructive form of tuberculosis begins to develop the areas of disease are microscopic and therefore do not cast visible shadows on roentgenograms. However, as these areas enlarge and develop sufficient consistency, their locations can be detected by the shadows they cast on roentgenograms. From this point on they evolve so slowly that it is an average of two or three years before they cause symptoms. This is often referred to as the silent stage because the host is unaware of the presence of the condition. However, it is during this stage, preferably in its early part, that the disease can nearly always be stopped from further progress. This can be done before it has become communicable and when it is still minimal in extent. When found at this time there is no disability, and therefore rehabilitation is not required. Usually successful treatment can be administered outside the hospital or sanatorium at relatively small expense.

Tuberculosis can be eradicated. Tuberculosis has never been at such low ebb in the United States as in recent years. Therefore, there has never been such an ideal time to move forward to the eradication goal. It would be extremely detrimental to the eradication program if there were any slacking of effort when the percentage of tuberculin reactors among grade school children reaches 1% and less. Indeed, the work must continue over a considerable time after the goal is initially attained of no reactor child in a school system. A single reactor means that a tuberculosis problem still exists. This fact has been emphasized many times by the veterinary profession in its nationwide tuberculosis eradication campaign among cattle. In one state where the disease was reduced to 0.1%, as manifested by the tuberculin test among cattle, complacence resulted in relaxation of effort and in a few years the disease had returned and attained a high level.

In most parts of the United States the control of tuberculosis has been so well accomplished that the eradication goal can now be visualized. The only time when the eradication campaign can begin is infancy. All babies are free from tubercle bacilli at birth. The tuberculosis eradication goal will not be reached until one generation of infants after another go through the span of life free from tubercle bacilli. This necessitates an environment free from liberated tubercle bacilli. In many areas of this country such environments have been provided for all but a fraction of 1% of children up to the age of 6 years. Indeed, there are areas where the ideal situation has been attained up to this age. The certification of schools project was designed to carry such children from kindergarten through 12th grade in a state of freedom from tubercle bacilli.

Program must be one of coordination and cooperation. No individual or single organization or group of professional workers can solve all the problems leading to eradication of the tubercle bacillus. All organizations and the entire citizenry must cooperate in a thoroughly coordinated program. Veterinarians are exceedingly important in the tuberculosis eradication program. They

are just as interested in and as willing to help eradicate this disease from people as persons in any other segment of the citizenry. Indeed, they know more about the tuberculin test and eradication measures than any other group of people in the world. They administered the tuberculin test to the cattle of this country 441,716,627 times from 1917 through the fiscal year 1963. They did postmortem examinations on the 4,144,891 reactors, thus determining the significance of the tuberculin reaction.

To achieve the desired accomplishment, the area to be included should be divided into small units, each with adequate organization, to insure complete coverage of its citizens periodically. The success of the program depends largely upon how well the citizens are informed. Tuberculosis and health associations have a dominant role to play because they are in the best position to disseminate important practical information about tuberculosis and thus insure area-wide support and cooperation. It must be remembered that department of health officials are the only persons in any community who have legal authority in the tuberculosis eradication program; thus, their unqualified support is indispensable. Inasmuch as only physicians are licensed to give or supervise administration and reading of tuberculin tests and make diagnoses, the importance of the role of the 275,000 physicians in various medical categories, including nearly 100,000 in general practice, is obvious. In adequately testing the 190 million citizens of the United States and conducting the subsequent epidemiologic work, the nursing profession will play an ever-increasing role.

Presented before the School Nurses Section, 110th Indiana State Teachers Convention, Indianapolis.

This paper is included in the James J. Waring Series because of Dr. Waring's fine appreciation of the importance of the nursing profession in eradicating tuberculosis.

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Penicillin Skin Test Procedure and Prevention of Penicillin Reactions

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INTRODUCTION

PENICILLIN HYPERSENSITIVITY is a doctor's dilemma. According to a recent estimate by Feinberg,[1] as many as 300 persons may die each year in the United States as a result of penicillin anaphylaxis. This would be especially tragic in the case of a young adult beginning his years of productivity. For this reason a penicillin skin test procedure was introduced in Northwestern University student health service, in 1955, by the consulting allergist.* For the past eight years a scratch test for hypersensitivity has been done before the administration of either oral or parenteral penicillin.

The student health service provides complete health care for approximately 6,700 young adults, including outpatient services and bed care. Annual surveys have indicated that 90 to 93% of the students used the health service with an average of 4 outpatient visits per year.

MEASURES TO REDUCE REACTIONS

1. Penicillin is not given to patients with a history of penicillin reaction. The medical history obtained on admission to the university includes a question regarding drug allergies. If the student indicates an allergy, a red-lined label indicating drug sensitivity is placed on the outside of his record folder, and the student is given a wallet card bearing this information.

Table 1 shows the incidence of penicillin allergies in new students. It is noted that the incidence during the past three years is about 6% for young adults entering college. Olsen[2] reports 3.6% in young military inductees in 1957. It is possible the students represent a group with more opportunity to receive penicillin during their previous years.

When hospitalized in the infirmary, our admitting procedure includes a question regarding allergies. When a physician considers using penicillin he will determine anew whether there is any possibility of previous reaction to penicillin.

2. Penicillin treatment is avoided if possible in patients with an allergic constitution. These patients are candidates for eventual penicillin sensitivity.[3] Collins[4] reported 4 times as many reactions in allergic children. Brown[5] reported 3 times as many reactions in allergic subjects.

3. Penicillin is given only when necessary. The great dilemma in student health work is the treatment of beta-hemolytic streptococcus respiratory infections in which penicillin is the recommended first choice. Careful attention is paid to this diagnosis and the risk of infection weighed against the risk of reaction.

4. Nothing that is effective by mouth should be given by injection. Oral penicillin seems less dangerous than parenteral. However, Batson[6] advises that "one still must be wary of acute reactions after oral therapy and such treatment should always be started in presence of a physician."

5. All patients are kept in the building for twenty minutes after injections. This permits immediate recognition and emergency treatment of reactions. Drugs and equipment must be accessible at a moment's notice in an emergency kit. This step may account for increased awareness and increased incidence of mild immediate reactions in our statistics.

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TABLE 1

HISTORY OF PENICILLIN ALLERGIES ON ADMISSION TO THE UNIVERSITY

Year	*No. of new students*	*No. of penicillin allergies*	*Percentage*
1963	2680	178	6.64
1962	2652	160	6.03
1961	2688	178	6.62

6. Care must be used in avoiding intravascular entry when giving intramuscular injections. A wide bore needle (21 gauge) is necessary to permit aspiration of blood with prolonged traction. If position of needle is changed, repeat traction is necessary. If blood is seen in the syringe a new site must be selected.

7. Syringes and needles for penicillin therapy are not used for other material. Coleman[7] demonstrated that traces of penicillin are difficult to remove and evoke reactions in a sensitive patient.

8. Health education is necessary to help our patients appreciate careful use of drugs; many believe that penicillin is a panacea for all illness. It is also a common belief that having had penicillin previously without reaction indicates that none will occur the next time. There is a failure to understand that a previous primary sensitizing dose is necessary for reaction. This may have been inadvertently obtained through milk, vaccines, fallout, or other inapparent contact. The patient is also advised that skin testing is only a guide and helpful if positive.

9. A penicillin skin test is done, by means of which an anaphylactic reaction may be avoided.

PROCEDURE

The scratch test is applied by a nurse trained in allergy. The skin is cleansed with 70% alcohol. With a scalpel, a linear scratch one-eighth inch in length is made through the epidermis of the volar surface of the mid-forearm. A drop of penicillin G procaine, 300,000 units per cubic centimeter in aqueous suspension, the most commonly used parenteral penicillin in the student health service, is placed on the scratch. The solution is allowed to remain on the skin for twenty minutes unless a reaction is noted before the time limit. If this should happen the penicillin should be washed off to prevent any further reaction. A control diluent on the other arm is used to eliminate any false-positive reactions due to possible irritating effect to the diluent and to the scratch itself, or both.

The reading of the skin test is done by the physician and reflects the immediate type of reaction to penicillin. A positive test consists of a wheal and erythematous flare, and it also indicates the possibility of an anaphylactic reaction occurring. A negative test does not eliminate the possibility of an anaphylactic reaction. It is known that penicillin-allergic patients may lose a marked degree of their skin sensitivity to penicillin and yet be systemically sensitive. This may occur within a few weeks to twenty-four months following their penicillin reaction.[2] Therefore, a positive skin test should be taken as a definite penicillin allergy and a reaction is likely to follow on subsequent injections, but a negative skin test does not exclude this possibility. One cannot learn anything regarding the possibility of a delayed penicillin reaction such as urticaria or serum sickness from the skin test.[1]

RESULTS

From 1955 to 1963, 1,527 penicillin skin tests and 2,169 penicillin injections were administered. Each patient is tested prior to penicillin treatment, either oral or parenteral. However, this is not repeated during consecutive therapy. Kern[3] states that subsequent doses in the same series of injections will not cause severe reactions if the first dose did not, provided the interval between doses of a series is not greater than four days. This program was initiated as a routine procedure, and no concurrent statistics were collected on positive or negative skin tests. However, a review of 1,562 graduating class records in 1963 showed 103 penicillin skin tests were done. Thirteen were positive. In other words, about 13% of the patients selected for penicillin therapy were rejected.

From our outpatient and hospital diagnostic files, 28 cases of penicillin reactions were diagnosed and treated during this period (Table 2). Of these, 14 had been skin tested and interpreted

TABLE 2

CHARACTERISTICS OF TWENTY-NINE REACTIONS FOLLOWING PENICILLIN THERAPY

Penicillin administration	*Student health service*	*Outside agencies*
No. of reactions	14	15
Skin test	14	0
Interpretation	14 negative	–
Delayed reaction	12	15
Immediate reaction		
Mild	2	0
Severe	0	1
Parenteral penicillin doses	2,169	*Less than 500
Incidence/1,000	6.5	

*Based on time of risk, thirty-six weeks of school compared with six weeks of vacation

as negative; 2 of these had a possible mild, immediate reaction, and the others were all of delayed type. This gives an incidence of less than 0.7% reactions to penicillin parenteral injections.

Fifteen reactions were treated at the health service, following penicillin therapy from other agencies without skin test. Usually these were initiated during the vacation period. The vacation period is approximately six weeks of the academic year. From this period, approximately 50% of the penicillin reactions in our series occurred. None of these patients had received penicillin skin testing prior to injection. The injections were given elsewhere than at the student health service. We do not know exactly how much penicillin was given, but we can assume it should be approximately one-sixth of our total injections, or 360 injections. This gives an incidence of 3.7% reaction to penicillin without skin testing compared to 0.7% reaction with skin testing.

It is doubtful if we would have knowledge of the mild, immediate reaction which occurred in those treated outside of the health service. It is interesting to note that of the 28 patients who reacted to pencillin, 9 gave a family history of allergy and 5 had a personal history of allergy. Review of various authors[5,8–11] indicates an incidence of penicillin reaction in series from 0.9% to 10%. Brown[5] estimates injected penicillin will cause some reaction in 5% of non-allergic adults and in 15% of allergic subjects.

The scratch skin test procedure has been safe. There have been no systemic reactions to the scratch tests.

Case reports of the 3 patients who had immediate reactions to penicillin therapy during this period are presented.

CASE REPORTS

Case 1. The patient had a negative skin test and received 600,000 units of procaine penicillin G aqueous solution. In fifteen minutes the patient reported feeling dizzy and nauseated. No treatment was given since recovery was immediate. This was diagnosed as a possibly mild, immediate type reaction.

Case 2. The patient, with hay fever history, was being desensitized with ragweed pollen. A family history of hay fever and asthma was obtained. In September 1957, he was being treated for cellulitis of the left popliteal area which was not responding to management. Penicillin scratch test was performed and was negative. He received 600,000 units of penicillin intramuscularly and immediately complained of a "funny feeling which became worse in his head." Breathing and pulse were rapid, skin was pale and cool. He was treated with adrenalin, 0.5 cc. 1:1000 aqueous, and chlorpheniramine maleate (Chlor-Trimeton), 10 mg. parenterally. Recovery was immediate, and the patient was hospitalized because of the infection of the popliteal area. This was diagnosed as a mild, immediate reaction.

Case 3. There was no prior skin test. An emergency call was received at the student health service stating a student had collapsed in a nearby university building. A doctor arrived at the scene and learned that the patient fell 2 times, cutting his forehead and lip. He thrashed about for a few minutes and became still. On examination a blood pressure was not obtainable; in fifteen minutes it was 60/50 with a pulse of 100. The patient was admitted to the hospital for observation. On recovery, he stated his skin felt prickly and warm, his nose was stuffy, and he thought this was an allergic reaction. It was discovered he had taken 200,000 units of oral penicillin twenty minutes prior, prescribed by a dentist because of an infected tooth. He had known allergies to trees, pollen, and dander.

Although the initial diagnosis was seizure state, there was no neurological evidence of epilepsy. Passive transfer tests performed revealed a strong sensitivity to penicillin. Crystalline penicillin G, 0.0018 unit, gave a positive transfer test, and diagnosis was made of severe immediate penicillin reaction to oral penicillin. Patient was advised to avoid all penicillin, and poliomyelitis vaccine. Final diagnosis was severe, immediate penicillin reaction.

DISCUSSION

The value of skin test for penicillin allergy has been controversial.[12–18] Almost everyone agrees that a positive test will provide information of the immediate type of reaction. The fact that an anaphylactic reaction may occur in spite of a negative scratch test makes the doctor wary of using it. It would seem, however, that any step taken to lessen the possibility of a life-threatening reaction is desirable. Not only is the interpretation limited, but there is no conformity in the methods and materials used.[19,20] New methods of detecting penicillin allergy include the development of a degradation product of penicillin, penicilloyl, which conjugated with polysine is being evaluated as a skin testing agent (Penicilloyl polylysine [PPL]).[21]

CONCLUSION

A skin testing program as a screening test for penicillin allergy has been carried out effectively in a busy outpatient department. The reaction rate is proportionately less than in a small group receiving penicillin from other sources without testing. Incidence of penicillin allergy on the admission to the university, based on past history, is about 6%. The reaction rate to parenteral penicillin under this program is 0.7%. There has been no untoward reaction to the penicillin scratch test. The procedure is considered to be a basic measure in prevention of anaphylactic penicillin reactions.

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Bronchial Obstruction from Aneurysm of the Pulmonary Artery Associated with Absence of the Pulmonary Valve

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CONGENITAL ABSENCE of the pulmonary valve is a rare lesion which refers to agenesis or hypoplasia of the pulmonary valve cusps.[1] It is generally associated with aneurysm of the pulmonary artery. Congenital pulmonary valve insufficiency results from absence of the pulmonary valve, or on occasion may result from idiopathic dilatation of the pulmonary artery, or a quadricuspid or bicuspid pulmonary valve.[2] A recent review of the literature since 1908[3] revealed 38 cases of congenital pulmonary valve insufficiency, 27 of which had an associated ventricular septal defect. Twenty of these 27 cases with ventricular septal defects were associated with the tetralogy of Fallot.

Isolated congenital pulmonary valve insufficiency may be compatible with cardiac competence until adult life.[4] Studies in experimental animals following postnatal total pulmonary valvectomy indicate that the condition is well tolerated.[5] The right ventricle can maintain an output several times normal for a long period of time without failing as long as the pulmonary artery pressure remains low. In the fetus, however, the pulmonary artery pressure and the systemic pressure are at the same level and the ductus arteriosus is patent. Regurgitant flow in the fetus occurs, therefore, during ventricular diastole. In addition, it has been speculated that aortic blood may enter the pulmonary artery through the patent ductus and increase pulmonary regurgitation.[6] These factors produce great strain on the right ventricle in utero and during early infancy. The presence of an associated ventricular septal defect adds further to the work load of the right ventricle and may bring about heart failure in an infant who might otherwise have survived the period of transition to a lower pulmonary artery pressure.

The following case of aneurysm of the pulmonary artery with absence of the pulmonary valve and a ventricular septal defect is reported to emphasize this entity as a cause of bronchial obstruction and heart failure in the newborn period.

CASE REPORT

I. K., 34-55-78, was born at 8:35 A.M. on October 10, 1963. There were no prenatal maternal complications. The infant was "slow to breathe and had a dusky appearance" at delivery. The heart rate was 160 per minute and the respiratory rate 45 per minute. A systolic precordial cardiac murmur was heard shortly after birth. A chest roentgenogram (Fig. 1) "suggested cardiac enlargement and a mediastinal mass." At 12:00 P.M. on the first day of life, the liver was noted to have enlarged and the respiratory rate continued at 40-50 per minute. Digitalis was given at this time. On the morning of Oct. 11th, a continuous murmur was heard over the left chest.

The patient was transferred to the Indiana University Medical Center in the afternoon of Oct. 11th. At the time of admission, the patient appeared critically ill. Cyanosis was noted around the mouth. Heart rate was 30 per minute. Systolic and diastolic murmurs were heard over the left precordium and there was dullness to percussion over the left hemithorax. The liver was enlarged 4 cm. below the right costal margin. Chest roentgenograms (Fig. 2) at this time indicated atelectasis of the upper lobe of the left lung and narrowing and retrodisplacement of the trachea. The cardiac silhouette was enlarged and there was suggestion of a right aortic arch. Congenital heart disease with a mediastinal mass or pulmonary artery aneurysm was the roentgenologist's impression. A repeat bedside roent-

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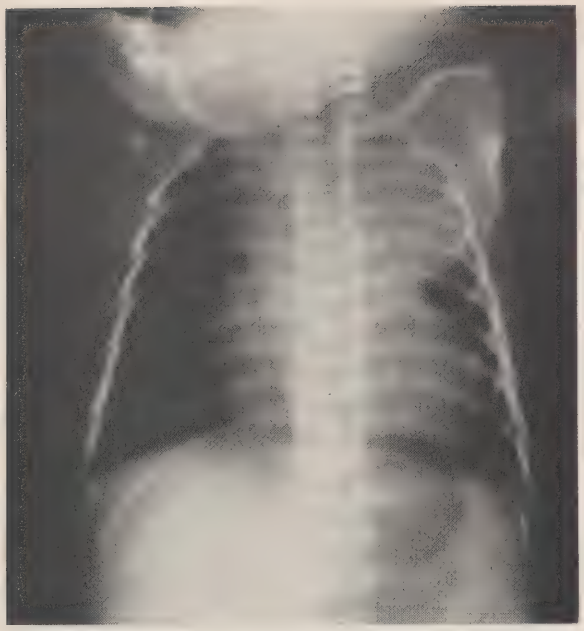


Fig. 1. Frontal chest roentgenogram exposed on the first day of life. There is cardiac enlargement and a large mediastinal density representing the pulmonary artery aneurysm and perhaps some thymic tissue. There is reduced aeration of the upper lobe of the left lung. The aortic arch is on the right. Postmortem study thirty-six hours later indicated atrophy of the thymus.

genogram six hours later indicated total atelectasis of the left lung (Fig. 3).

Death occurred late in the evening of Oct. 11th. Postmortem study revealed an infant weighing 2,780 gm. There was atelectasis of the left lung and atrophy of the thymus. The heart was not weighed. The right atrium was dilated. The tricuspid and mitral valve leaflets were not remarkable nor were the aortic cusps. The pulmonary cusps were absent as such and in their place were several small tags. The circumferential measurements of the valve orifices were: tricuspid 3.4 cm., pulmonary 2.2 cm., mitral 2.3 cm., and aortic 2.3 cm. The right ventricular wall was 0.4 cm. in thickness and the left ventricular wall 0.5 cm. The foramen ovale was probe patent. A 0.7 × 0.9 cm. defect was present in the membranous portion of the interventricular septum. The aorta arose from the left ventricle and the aortic arch was on the right. The pulmonary artery arose from the right ventricle. Beyond the pulmonary orifice, the pulmonary artery and its right and left branches were present in the form of a dilated "T" shaped sac measuring 2.5 × 3 × 1.5 cm. (Fig. 4). This sac compressed the lower portion of the trachea and both main stem bronchi. A ductus arteriosus or ligamentum arteriosum was not found. Microscopic analysis of the tags present in the region normally occupied by the pulmonary valve cusps indicated "myxomatous connective tissue." Sections through the aneurysmal pulmonary artery did not indicate the presence of cystic medial necrosis. There was acute passive congestion of the liver, spleen, and kidneys.

COMMENT

This newborn male infant developed congestive heart failure in the first 4 hours of life. A chest roentgenogram made during this period indi-

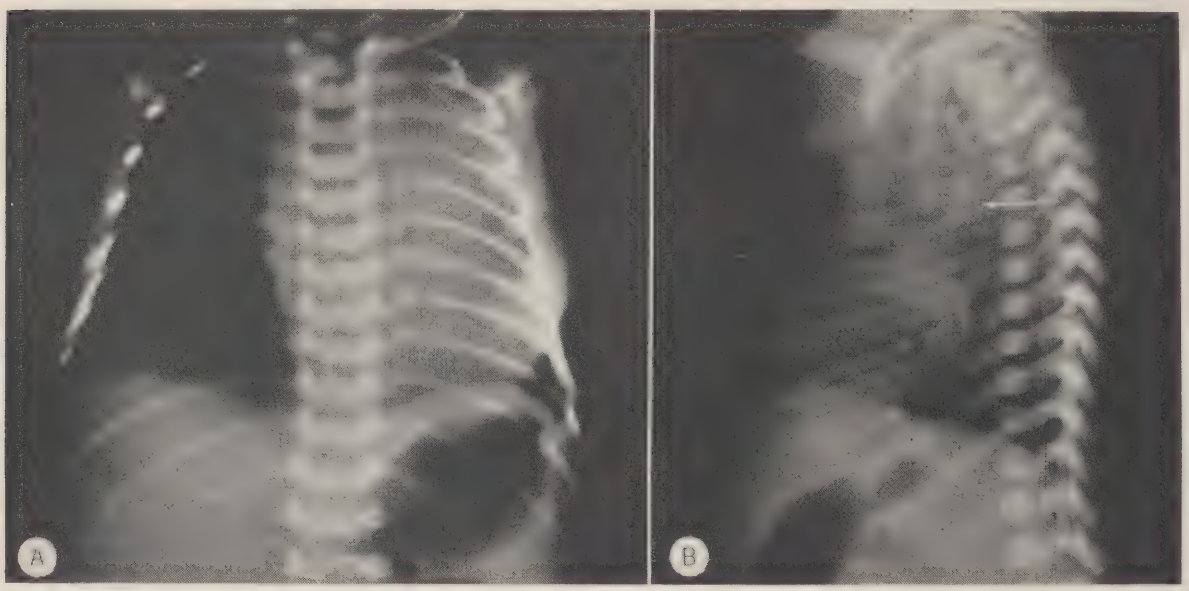


Fig. 2. (A) Frontal chest roentgenogram at 30 hours of age indicating atelectasis of the upper lobe of the left lung and cardiac enlargement. (B) Lateral chest roentgenogram at 30 hours of age indicating narrowing and retrodisplacement of the trachea (arrow) by the aneurysmal pulmonary artery.



Fig. 3. Frontal chest roentgenogram at 36 hours of age indicating total atelectasis of the left lung.



Fig. 4. The thoracic viscera as seen at postmortem. The smaller upper arrow points to the orifice of the markedly dilated right pulmonary artery which is continuous with the aneurysm of the main pulmonary trunk (lower larger arrow). The pulmonary valve ring has been removed in part for histologic study.

cated cardiac enlargement and an oval superior mediastinal soft tissue density which extended into the projection levels of the right and left upper lung fields. Bedside chest roentgenograms at the time of admission to the Indiana University Medical Center at 30 hours of age indicated atelectasis of the left upper lobe and cardiac enlargement. A lateral projection of the chest at this time suggested posterior displacement of the trachea with severe narrowing of the lower two-thirds. A right aortic arch was also evident. Six hours later, a repeat chest roentgenogram indicated total atelectasis of the left lung.

DISCUSSION

Miller and associates[7] reported 7 patients with absence of the pulmonary valve associated with infundibular pulmonic stenosis, ventricular septal defect, overriding of the aorta, and aneurysm of the pulmonary artery. The 3 youngest patients in this group (2 months, 7 months, and 3 years) had striking symptoms of respiratory obstruction. In 2 of these, a markedly dilated pulmonary artery compressed the left main stem bronchus to produce obstructive emphysema of the left lung and a shift of the heart and mediastinum to the right. These authors suggested that the pulmonary artery aneurysm may have resulted from a congenital muscular weakness at the base of the pulmonary artery.

Several reports of absence of the pulmonary valve have emphasized the presence of a very large main pulmonary artery visible on the frontal chest roentgenogram as well as prominence of the right pulmonary artery.[3,8] The patient herein described was similarly affected in that an aneurysm was present in the region normally occupied by the main pulmonary trunk and the right and left pulmonary arteries. The peripheral pulmonary vasculature in this patient was slightly exaggerated.

The features which characterize absence of the pulmonary valve and ventricular septal defect are: (1) harsh, to-and-fro, systolic-diastolic murmurs and thrills along the left sternal border, (2) electrocardiographic changes consistent with right atrial enlargement and right ventricular hypertrophy, and (3) chest roentgenographic and roentgenoscopic findings of cardiac enlargement, and a large pulsatile main pulmonary trunk with large pulsatile right and left branches. In addition, there may be signs of obstructive emphysema of the left lung[7] or complete atelectasis. The major roentgen finding of a large or aneurysmal main pulmonary trunk may be obscured in the presence of atelectasis of the left lung but the clinical features along with tracheal narrowing and retrodisplacement should suggest the correct diagnosis.

SUMMARY

A newborn infant with atelectasis of the left lung from bronchial obstruction by an aneurysm of

the pulmonary artery is reported. The pulmonary artery aneurysm is associated with absence of the pulmonary valve and a ventricular septal defect.

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Penicillin Skin Test Procedure and Prevention of Penicillin Reaction

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Left Aortic Arch and Right Descending Aorta

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THE COMBINATION of left aortic arch and right descending aorta is a rare vascular anomaly. Only 6 cases have been documented since Paul's first description of 2 cases in 1948.[1]

It seems, therefore, worthwhile to report our recent experience with 1 such case.

CASE REPORT

A 51-year-old male was admitted to Deborah Hospital in March 1964, with the complaint of shortness of breath. He had been known to have a heart murmur for approximately eleven years. Over the past two years there had been a progressively increasing dyspnea, and of late he had been suffering from frequent paroxysmal nocturnal dyspnea and considerable fatigability. There was no history of rheumatic fever, swallowing disturbance, wheezing, or ankle edema. He had been treated for diabetes mellitus for a year. Four years prior to admission the patient was involved in a car accident which resulted in rib fracture and hemothorax.

Physical examination revealed the patient in no apparent distress at rest. The blood pressure was 120/70 mm. Hg. The radial pulse was regular at 70 per minute, not of Corrigan type in quality. The maximal apical impulse was felt in the fifth intercostal space slightly to the left of the left midclavicular line. A_2 was diminished and an early blowing diastolic murmur of grade 4/6 was heard all over the precordium, best along the left sternal border and at the aortic area. An ejection murmur of grade 4/6 was heard best at the aortic area with radiation toward the neck. The lungs were clear to percussion and auscultation. The liver was not palpable. No peripheral edema was demonstrable. Physical examination was otherwise not remarkable.

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An electrocardiogram showed normal sinus rhythm at 68 per minute, normal conduction, Ā QRS + 5°, and left ventricular hypertrophy with strain pattern (Fig. 1).

Fluoroscopy and routine posteroanterior roentgenography of the chest with barium swallow demonstrated pleural thickening in the right base, as well as evidence of old rib fractures involving sixth to ninth on the right side. The cardiac silhouette was characterized by overall enlargement of 2+, prominent aortic knob, and a double contour of the right border (Fig. 2). The right anterior oblique and left anterior oblique projections revealed an anterior displacement of the esophagus at the level of the seventh vertebra (Figs. 3 and 4).

On retrograde aortography, the catheter was seen along the left border of the vertebral column throughout the course of the abdominal aorta. It then entered what appeared to be the

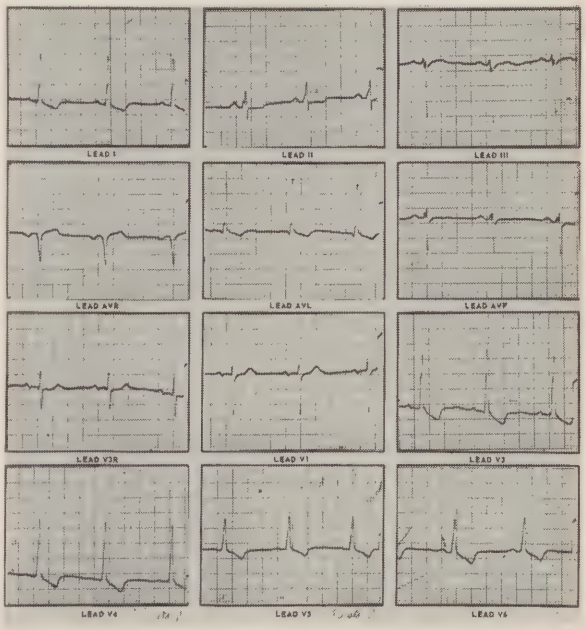


Fig. 1

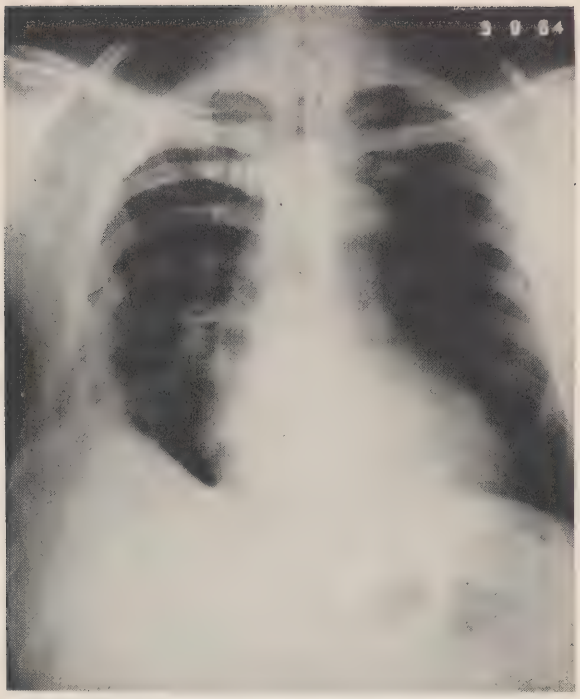


Fig. 2. Posteroanterior projection. Note left aortic arch, prominent aortic knob, and double contour of right border of cardiac silhouette.

right atrium as if it had been introduced into the right femoral vein instead of the right femoral artery. A blood sample was obtained and was proved to be arterial. Further advancement of the catheter into the left ventricle was not successful because of marked tortuosity of the vessel over a long segment. With the tip of the catheter at the root of the aorta, 40 cc. of diprotrizoate sodium (Ditriokon®) were injected. The ascending aorta was seen directed cranially to the left to form a left aortic arch which, after having given off the left common carotid artery and the left subclavian artery, turned posteriorly, then caudally and to the right, and crossed the vertebral column at the level of the seventh vertebra (Fig. 5). An aortic regurgitation of 2+ was also observed. The aortic, as well as femoral arterial curve, revealed a wide pulse pressure and absence of the dicrotic notch.

The anomaly was confirmed at the open heart surgery for correction of aortic regurgitation.

DISCUSSION

Three findings characterize the described anomaly, namely: (1) left aortic arch, (2) anterior displacement of the esophagus due to retroesophageal passage of the aorta, and (3) right descending aorta which, in our case, simulated double cardiac contour.

While awareness of this anomaly might have led to the diagnosis by characteristic chest X-ray findings alone, had it not been for the retrograde aortography, these would have been overlooked. It is interesting to note that the initial position of the catheter in the cardiac silhouette was such as



Fig. 3. Right oblique anterior projection. Note anterior displacement of esophagus.



Fig. 4. Left oblique anterior projection. Note anterior displacement of esophagus.

TABLE 1

	Reported by	*Age*	*Sex*	*Clinical manifestation*	*Associated anomaly*	*Diagnosis by*
1	Paul (1948)	7	F	Those related to tetralogy of Fallot	Tetrology of Fallot	Roentgenogram and confirmed at thoracotomy
1	Paul (1948)	11½	M	Those related to tetralogy of Fallot	Tetrology of Fallot	Roentgenogram and confirmed at Blalock's operation
2	Edwards (1948)	17 months	M	Mild dysphagia		Autopsy
3	Heinrich and associates[3] (1956)	50	M	None		Roentgenogram
4	Heim de Balsac (1960)	77	M	Those associated with aortic regurgitation		Roentgenogram
5	Schlamowitz and associates[5] (1962)	17	M	No cardiorespiratory or GI symptoms	Persistent left superior vena cava	Roentgenogram, selective angiogram, selective aortogram

to raise a question of this being in the right atrium.

Unlike Edward and Schlamowitz, we were not able to demonstrate a vascular ring in this case.[2,5]

Of the previous 6 patients, there was only 1 who presented a symptom attributed to this anomaly, namely, mild dysphagia (Table 1).[2]



Fig. 5. Retrograde aortogram. Note left aortic arch and right descending aorta.

Further experience with similar cases may disclose a variety of symptoms hitherto unknown. It is conceivable that depending on the severity of encroachment on the esophagus and trachea by the encircling vascular ring, significant compression symptoms may present themselves and warrant surgical correction. This might be particularly so in old age when the vessels widen and produce more compression of the esophagus and trachea.[2] Relief of symptoms may well be accomplished, as in right aortic arch and left descending aorta, by surgical division of the ligamentum arteriosum.

SUMMARY

A case of left aortic arch and right descending aorta, believed to be the seventh reported case, is presented. The anomaly was found in a 51-year-old male during cardiac catheterization and aortography for evaluation of aortic valvular disease and was subsequently proved at aortic valvular surgery. Although initially unrecognized in their significance, the characteristic findings were present in the chest films. The lesion itself caused no symptoms.

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Juvenile Pulmonary Arteriopathy Due to Pulmonary Hypertension

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THE CONCEPT of pulmonary arteriopathy as a sequel of pulmonary hypertension has become established in recent years.[1–9] In patients with this syndrome periarteritis-like lesions of the medium- and small-size arteries are found solely in the lungs. They are considered not to be due to a primary arteritis but to segmental necrosis of the arterial walls with ensuing inflammatory reaction. This paper describes such a patient in whom the arterial lesions were particularly extensive and advanced.

CASE REPORT

The patient was aged 3½ years at the time of his death. His twin brother had developed normally and was of average intelligence. He was mentally backward, had a pigeon chest, and had been admitted to the hospital on several previous occasions for asthma and repeated attacks of bronchopneumonia. He was finally admitted the day before death, critically ill and very dyspneic, with a normal temperature, a pulse rate of 130 per minute, and an enlarged heart. A chest radiograph also showed a large heart shadow and diffuse, small nodular opacities throughout both lung fields. Laboratory investigations showed: hemoglobin, 40%; white blood count, 21,600, with polymorphs predominating; and erythrocyte sedimentation rate, 150 mm. after one hour.

Necropsy. This was carried out forty hours after death. Significant abnormalities were confined to the thorax. The pericardial sac contained 20 cc. of clear serous fluid. Both pleural sacs were obliterated due to widespread fibrous adhesions. The thymus was small, weighing 5 gm. (normal 23 gm.). There was a large cor pulmonale weighing 170 gm. (normal 65 gm.), the left side forming a mere appendix to the right. The wall of the left ventricle measured 0.8 cm., and that of the right was 0.9 cm. in diameter. The foramen ovale and the ductus Botalli were closed. There were no congenital abnormalities of the heart, coronary arteries, or large vessels. The myocardium was red and firm. The bicuspid orifice measured 7 cm., the tricuspid 7.5 cm., the aortic 3.2 cm., and the pulmonary orifice 4.4 cm. in circumference. Both pulmonary arteries were of large caliber. The lungs were normal in shape, enlarged, plum-colored, and consolidated, weighing together 700 gm. (normal 175 gm.). Many small, firmer, and lighter colored areas were present at their peripheries. The hilar lymph glands were grossly enlarged, edematous, and congested.

Bacteriologic and viral examinations. Swabs were taken from both lungs, but no growth was obtained on ordinary culture. No virus was isolated on tissue culture and embryonated eggs of specimens from both lungs.

Microscopic examination. Multiple blocks were cut from all lung lobes. The small, peripheral, light colored areas are recent infarctions. There were many areas of bronchopneumonia throughout, and occasional small groups of siderophages were present within alveoli. The large pulmonary arteries were thick walled and possessed grossly thickened elastic coats of systemic type. The medium-size arteries were also thick walled and muscular, and by far the greater proportion was diseased. The early acute lesions showed patchy fibrinoid necrosis of their muscular walls of varying extent. The subacute lesions displayed, in addition, destruction of elastic coats and annular or crescentic infiltration of thickened intima and adventitia by numerous neutrophils and lymphocytes, which also transmigrated the necrotic muscle coat (Figs. 1, 2, and 3). Fresh thombus frequently occluded the distal vascular lumina, thus accounting for the peripheral areas of infarction.

The older lesions were quiescent, without cellular reaction. The arterial walls, sometimes

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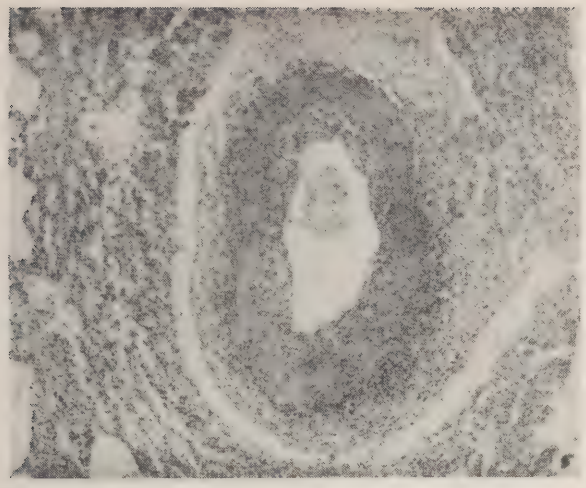


Fig. 1. Acute lesion. Cross section of small pulmonary artery displaying fibrinoid necrosis of muscular wall with inflammatory infiltration of adventitia and thickened intima. Hematoxylin and eosin, × 67

displaying aneurysmal dilation, exhibited an almost complete destruction of their elastic and muscular coats which were replaced by fibrous tissue. The lumen had been filled with fibrosing or fibrosed granulation tissue, often leaving a small patent channel, and sometimes revascularization by many small capillaries was discernible (Figs. 4 and 5).

Of the small arteries a proportion was not diseased; others displayed patchy fibrinoid necrosis. There were very few arterioles with thin walls and large lumina of the type normally present after the first few months of life. Otherwise, the arterioles presented as small-caliber vessels with thick muscular walls and small lumina, measuring 60 to 90 μ in total diameter and about 20 to 40 μ across their narrow lumina.

The hilar lymph nodes showed marked congestion and edema. Sections cut from all other main viscera showed no significant changes.

DISCUSSION

Histologically the arterial changes described resemble those of periarteritis nodosa. Periarteritis nodosa, however, is a generalized disease involving many organs but commonly sparing the lungs.[7] Periarteritis nodosa entirely confined to the lungs is unknown.

Wegener's granulomatosis may be limited to the upper and lower respiratory system, but in this condition the vessels are only secondarily involved.[10,11] The main lesions in Wegener's granulomatosis and its associated fatal midline granuloma of the face are extravascular granulomas with much necrosis and often showing multinucleated giant cells.

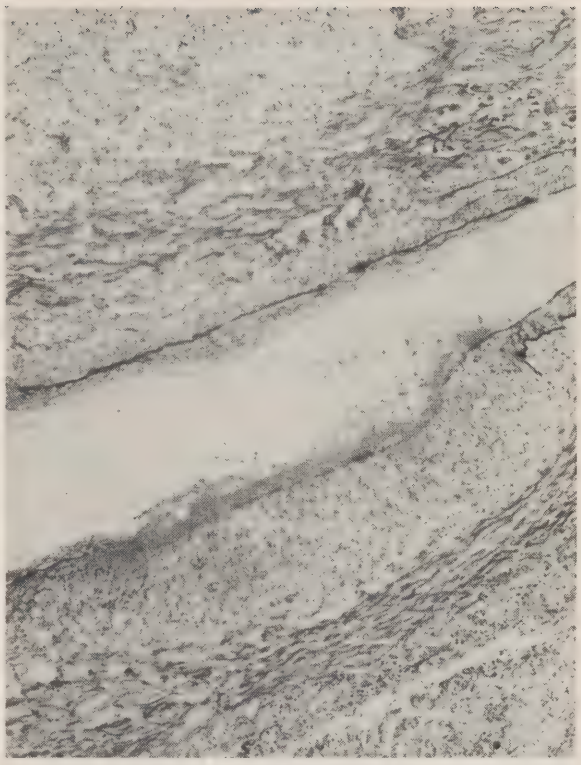


Fig. 2. Acute lesion. Longitudinal section of small pulmonary artery showing abrupt start of destruction of all coats. Verhoeff–van Gieson, × 67

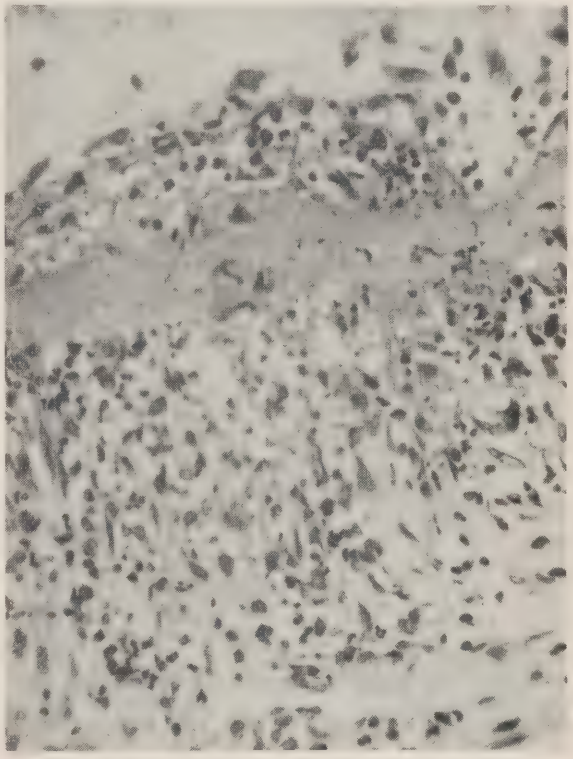


Fig. 3. Acute arterial lesion at higher magnification showing necrotic muscle coat and nature of inflammatory exudate. Hematoxylin and eosin, × 300

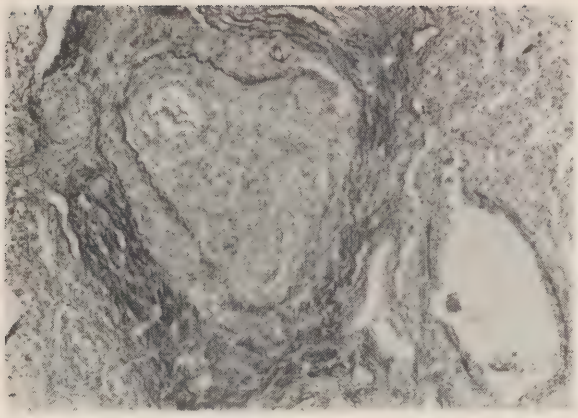


Fig. 4. Older arterial lesion. Moderate aneurysmal dilation, destruction of muscle and elastic coats, and small remaining lumen; remainder filled with fibrosed granulation tissue. Verhoeff–van Gieson, × 67

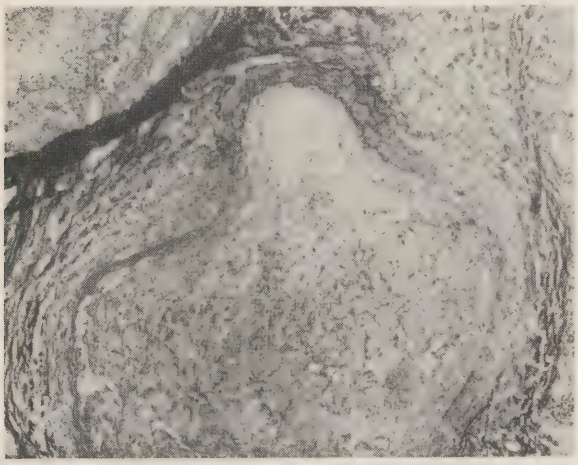


Fig. 5. Older arterial lesion with considerable aneurysmal dilation. Part of original vascular wall still recognizable. Small remaining patent lumen, remainder filled with loose granulation tissue displaying numerous small revascularized channels. (Black band at top left corner an artifact). Verhoeff–van Gieson, × 67

Thus, the restriction of the arterial lesions to the lungs rules out a diagnosis of periarteritis nodosa, and the absence of extravascular granulomas rules out a diagnosis of Wegener's granulomatosis. Hence, by exclusion, one is left with the concept of arteriopathy as seen in cases of pulmonary hypertension.

Chronic pulmonary hypertension can be due to a variety of causes that can conveniently be subdivided into 3 main categories: (1) passive hypertension, mainly due to acquired lesions, such as mitral stenosis, in which the venous drainage from the lungs to the left auricle is impeded, (2) hyperkinetic hypertension, which is due to congenital malformations of the heart or the great vessels causing a left-to-right shunt and resulting in a greatly increased flow of blood through the lungs, and (3) obstructive hypertension, caused by blood, parasitic or neoplastic emboli, thromboses, conditions producing fibrosis (such as sarcoidosis, Hamman-Rich syndrome, collagen diseases, and pneumoconioses), or vasoconstriction of smaller muscular arteries.

In all these conditions pulmonary hypertension may cause arterial necrosis, but in the majority of patients no such damage does occur, which is due to several factors. First, the pulmonary circulation can accommodate a threefold rise in pressure without leading to signs and symptoms.[12] Second, all these conditions give rise to a gradual increase in pulmonary arterial pressure, and the peak reached usually remains below a critical level. Third, the rapidity of the rise in blood pressure is of paramount importance.[13] Thus a chronic pulmonary hypertension will usually not produce any arterial damage unless there is a sudden exacerbation, as caused, for example, by vascular spasm due to anoxia.

Anoxia is regarded as perhaps the most powerful vasoconstrictor and may, in cases of chronic pulmonary hypertension, be caused by a superimposed pulmonary infection. In conditions of hypersensitivity, such as in asthma, histamine is released, and histamine is likewise a powerful vasoconstrictor.

In the present case definite evidence was obtained at necropsy of pulmonary hypertension. There was a marked cor pulmonale (in the absence of congenital cardiac or vascular malformations or of acquired lesions) and the larger pulmonary arteries possessed the elastic structure of systemic arteries. In addition, patchy bronchopneumonia was present which must have resulted in some degree of anoxia and, hence, in vascular spasm followed by fibrinoid necrosis of arterial walls. It should also be remembered that the patient was suffering from asthma, another condition leading to vascular spasm. These 2 factors would thus account for a sudden and critical further increase in the already raised pulmonary arterial pressure, setting in train the entire chain of lesions: localized arterial spasm, segmental arterial necrosis, inflammatory reaction (producing features histologically resembling periarteritis nodosa), thrombosis, and infarction, with organization of thrombi and recanalization in the older lesions, a process which would be self-perpetuating until the degree of anoxia would no longer be compatible with life.

There remains the problem of the primary pulmonary hypertension in the absence of any obvious cause. An adequate explanation for this can be advanced.[9,14,15]

In the newborn the small pulmonary arteries are thick-walled and muscular, with but a narrow lumen. In a matter of six to ten months these arterial lumina dilate very considerably, and the arterial walls lose their muscular coats and assume their permanent thin-walled proportions. If, for some unknown reasons, this postnatal transformation of the smaller pulmonary arteries should not take place this would inevitably lead to pulmonary hypertension. With few exceptions the small pulmonary arteries of the present patient were of small caliber and muscular and were of small bore. These findings are quite similar to those observed by Goodale and Thomas.[14] In view of the fact that the patient's symptoms developed soon after birth and had been present intermittently throughout his life the conclusion seems inescapable that the pulmonary hypertension in this instance was due to persistence of the fetal proportions of the small pulmonary arteries into postnatal life.

SUMMARY

A case of widespread and advanced pulmonary arteriopathy due to pulmonary hypertension is described in a boy aged 3½ years. The possible mechanism of the lesions is discussed. In the absence of any other abnormality, the persistence of the fetal type of small pulmonary arteries is advanced as a likely explanation for the pulmonary hypertension, with vasoconstriction due to anoxia and asthma as the reason for the pulmonary arterial lesions of periarteritis type.

I am greatly indebted to Prof. J. Gough and Dr. H. Spencer for their help in interpreting the features of this case. I am most grateful to Prof. R. A. Willis for reading the manuscript. Miss Phyllis E. Coleman was responsible for the photomicrography.

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ASSESSMENT OF THE SEVERITY of chronic ulcerative colitis is aided by examination of the peripheral blood smear. The most frequently seen hematologic changes are toxic granulation in the neutrophils, macrocythemia, moderate eosinophilia, myeloid immaturity, increased platelets, grade 2 or higher rouleau formation, and hypochromasia of erythrocytes. The most consistent finding in patients with associated chronic liver disease in macrocythemia, an uncommon finding in others. Positive lupus erythematosus cell tests may indicate coexistent disease or reaction to a drug such as salicylazosulfapyridine (Azulfidine) or hydralazine. Records of 23 patients considered seriously ill with chronic ulcerative colitis revealed toxic granulations in 17, myeloid immaturity in 14, increased platelets in 11, and grade 3 or 4 rouleau in 9. Macrocythemia was discovered in 5 of 11 patients with chronic liver disease.

RICHARD G. FARMER, M.D., HAROLD H. SCUDAMORE, M.D., and EDWIN D. BAYRD, M.D., Mayo Clinic and Foundation, Rochester, Minn. Amer. J. Gastroent. 41:601-610, 1963.

Lloyd S. Ralston, M.D.

C. H. PETERS, M.D.
Bismarck



DR. LLOYD S. RALSTON was born on a farm in Pembina County in northeastern North Dakota. His early education was in North Dakota and he received his B.A. degree from Mayville College, in Mayville, North Dakota, in 1939. The following two years he spent as a high school athletic coach and science instructor at Finley High School, Finley, North Dakota. He enrolled in the first-year class at the University of North Dakota School of Medicine from which he received his B.S. degree in medicine in 1943. He completed his undergraduate education at the University of Illinois and received his M.D. degree in 1944. He interned at the Garfield Park Community Hospital in Chicago where he came under the supervision of one of Chicago's leading internists, Dr. Ed Foley. This contact with Dr. Foley was extremely stimulating and undoubtedly has been the inspiration for much of Dr. Ralston's clinical astuteness and his exacting approach to the practice of medicine.

After serving in the United States Army for approximately two years, most of that time in Japan, he was discharged as a Captain in October 1947. At that time, he accepted a position as assistant professor of bacteriology and pathology at the University of North Dakota School of Medicine for the school year of 1947-1948. Following this, he was in general practice at Grand Forks, North Dakota, until 1950. In that year, he began his residency in internal medicine at the Veterans Administration Hospital in West Los Angeles and the University of California. In 1953 he returned to the Dakotas to practice internal medicine and was certified by the American Board of Internal Medicine in 1955. He became an associate professor of medicine at the University of North Dakota in 1960 and Chief of Staff at the Deaconess Hospital in Grand Forks. In the summer of 1962, he joined the medical staff of the Quain and Ramstad Clinic in Bismarck, where he has clearly demonstrated his profound knowledge of medicine and has continued to uphold and to improve upon high standards of medical practice.

He is a member of many professional organizations, a Fellow of the American College of Physicians, a member of the American Medical Association, Alpha Omega Alpha, and Sigma Xi. Dr. Ralston does not let medicine take all of his time, however, as he has excellent hobbies in photography and is an enthusiastic horseman who has won many blue ribbons throughout this area.

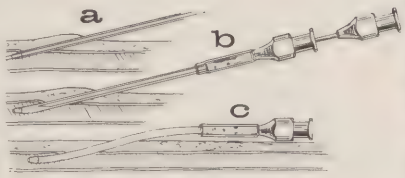
C. H. PETERS *is with the Quain and Ramstad Clinic, Bismarck.*

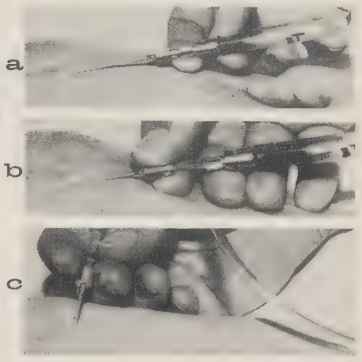
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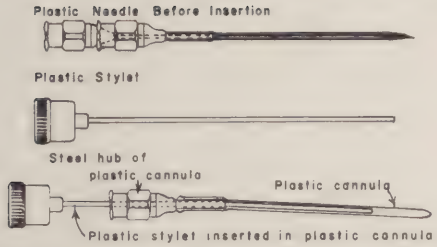




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Book Reviews . . .

A Practical Manual for the Treatment of Burns

by ELI RUSH CREWS, *119 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $6.75*

In his well-organized and lucidly written book, Dr. Crews gives the busy practitioner a systematic approach to the evaluation and treatment of the burned patient. The techniques of management are based primarily on the author's personal experience. For over ten years he has been chief of the burn service at the Robert B. Green (County) Hospital in San Antonio, Texas, and has had a special interest in the metabolic changes secondary to burns in infants and children.

Throughout the book the author emphasizes the physiological principles that underlie burn treatment. He stresses that a burn cannot be effectively treated by formula alone and offers a rather complete system for the evaluation of fluid requirements during the shock phase. In his scheme of colloid and electrolyte replacement, the urinary output serves as the most important index of treatment. Other chapters deal with general treatment of the burned patient from the second day onward and many of the problems that are encountered. There are separate chapters on nutrition and skin grafting. The final pages of the book are devoted to a detailed set of nursing instructions. These are written primarily for nurses and discuss, from their point of view, the various procedures and the rationale behind them.

This little manual contains a wealth of practical information and should be helpful to all physicians who take care of burned patients.

JAMES E. SEAY, M.D.
Minneapolis

Clinical Investigation in Medicine: Legal, Ethical and Moral Aspects

edited by IRVING LADIMER *and* ROGER W. NEWMAN, *517 pp., ill., Law-Medicine Research Institute, Boston University, Boston, 1964. $2.50*

The remarkable expansion of human experimentation, particularly in connection with clinical trials of new drugs, makes this anthology particularly helpful. It contains 73 selections from many different sources, with commentaries and various proposed principles of conduct or "codes" of ethics for human experimentation. It also gives legal information and surveys the recent federal laws in the United States regarding the testing of new drugs. Particularly helpful is a bibliography of over 500 references.

This volume represents an important contribution from the Law-Medicine Research Institute of Boston University, which was established in 1958 and which is directed by William J. Curran. Publication was aided by a grant from the Schering Foundation of Bloomfield, N.J., and this agency deserves thanks for its support.

The material is organized from the standpoint of historical and ethical perspective. Important essays are reprinted, such as those by H. K. Beecher on "Experimentation in Man," by M. B. Shimkin, and by O. E. Guttentag, in which there is discussion from the standpoint of research workers and of physicians on the problems of experimentation on human beings. Another section deals with attempted codifications, such as that of the Nuremburg Code, with commentaries on this document. Various codifications of American and international sources are also given. A wry note appears in the reprinting of a 1948 article by A. C. Ivy on the history and ethics of using human subjects in medical experiments.

A general legal commentary is offered with essays by many competent jurists, plus helpful religious and moral discussions by representative churchmen. The influential statement of Pope Pius XII on "The Moral Limits of Medical Research and Treatment" is given, with a consideration of medical ethics and morality. Clinical trials of new drugs are surveyed from the standpoint of legislation as well as from the newly developing discipline of clinical pharmacology. Scientific design and technique are discussed, with much commentary on patients and volunteers as subjects for experimentation. There is consideration of the use of prisoners, military personnel, and children for clinical investigation and discussion of the morality involved.

Altogether this is a useful volume that deals successfully with a very complex and difficult subject. Certainly it should be consulted by any biomedical scientist or clinician who proposes to undertake experimental studies on human beings.

CHAUNCEY D. LEAKE
San Francisco

Human Labor and Birth

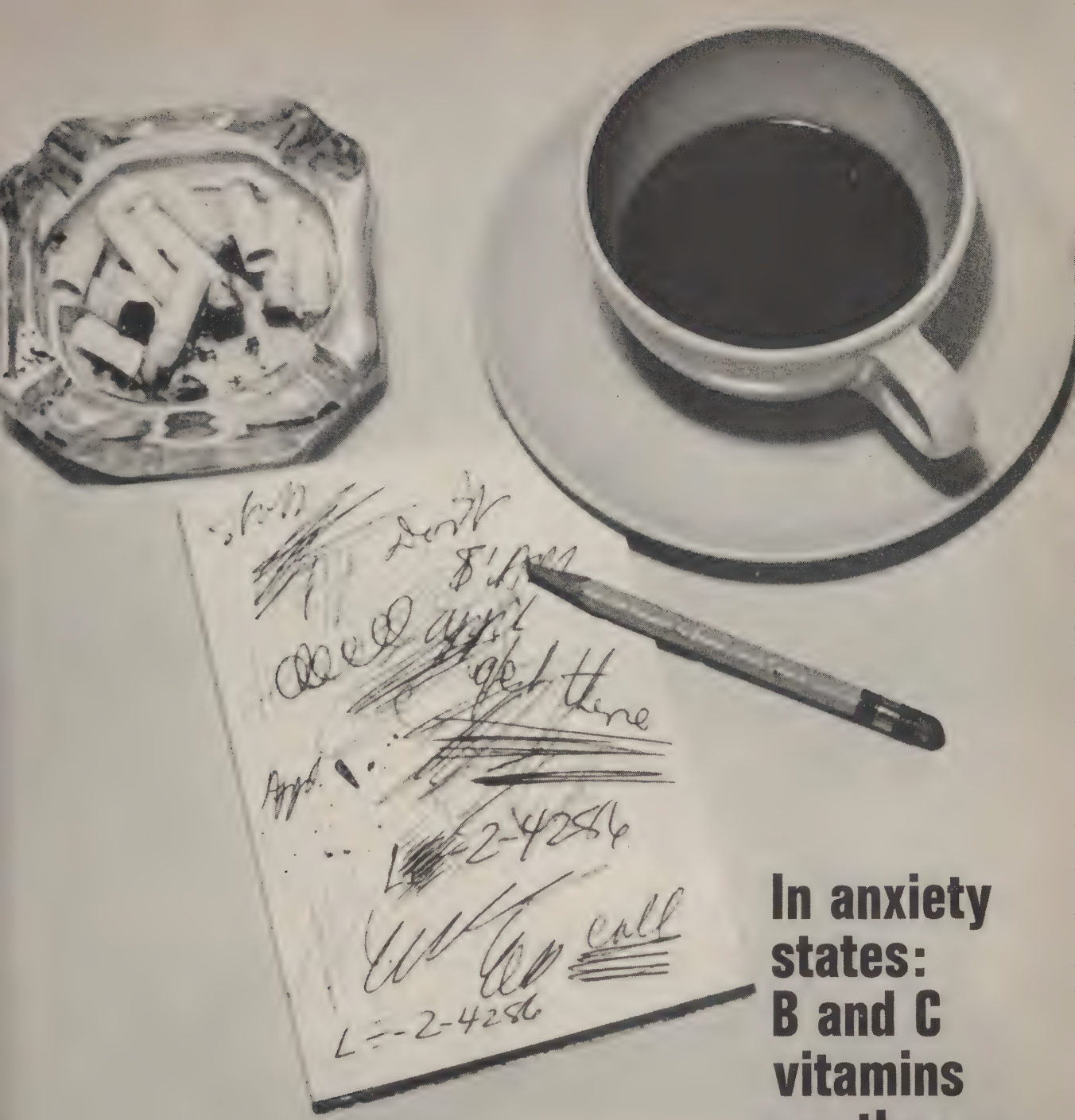
by HARRY OXORN *and* WILLIAM R. FOOTE, *485 pp., ill., Appleton-Century-Crofts, New York City, 1964. $7.95 (paperback)*

This first edition is directed primarily toward the particular needs of the medical student. With this goal in mind, the major purpose of the text, as stated in the preface, is to concentrate on the basic mechanisms and management of both normal and abnormal labor. The authors have succeeded extremely well in their avowed intention. The material is organized in a compact, concise, easily understood manner—in essentially outline form. All lengthy descriptions of complicated procedures are avoided, as are the biochemical, metabolic, and physiological changes observed in pregnancy. The accompanying illustrations, although certainly not all original, have been well chosen for their clarity and ability to supplement the text.

The contents are arranged into 42 chapters, ranging from the basic anatomy of the female pelvis through normal and abnormal labor. The numerous subdivisions and varieties of the latter are each discussed in detail via separate headings. The last 3 chapters of the book (Radiography in Obstetrics, Analgesia and Anesthesia, and The Newborn) comprise a wealth of pertinent material contained in relatively short summaries. Particularly informative are the sections dealing with breech presentation, shoulder dystocia, and intravenous oxytocin. Throughout the entire text information of a practical nature can be readily discovered. Such an example is the statement that the best treatment of compound presentation, in the absence of complications, is "masterful inactivity."

Nevertheless, entirely too much consideration is given

(Continued on page 16A)



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(Continued from page 14A)

to the intricacies of forceps applications, with unnecessary details for the ordinary medical student. Another minor criticism is the regrettable omission of the use of bilateral hypogastric arterial ligation as a lifesaving therapeutic procedure in postpartum hemorrhage (uterine atony). In addition, the statement that all breech presentations should have an attempt at external version is certainly open to disagreement.

Notwithstanding these minor points, the text, in summary, seems certain to be of practical value in its outline form not only to medical students studying for examinations but also for the busy practitioner confronted with every day obstetric problems.

HOWARD M. LEVINE, M.D.
Minneapolis

Tumors of Infancy and Childhood

by PAUL MICHAEL, *461 pp., ill., J. B. Lippincott Co., Philadelphia, 1964. $18.50*

After an introductory chapter on incidence, this book, based on an extensive volume of material, considers tumors according to the various body systems as they occur in infancy and childhood. Some of these tumors are like those seen in adults, while others have a tendency to be confined to the young.

The description of the various tumors is presented with clear language and is effectively supported by photomicrographs of high quality. A total of 309 figures represents very liberal illustration of the characteristics of many of the neoplasms considered. Each chapter is concluded by a concise and well-selected bibliography. This remarkable presentation will serve as a very useful reference for all concerned with sick infants and children, whether it be from the clinical or laboratory point of view.

JESSE E. EDWARDS, M.D.
St. Paul

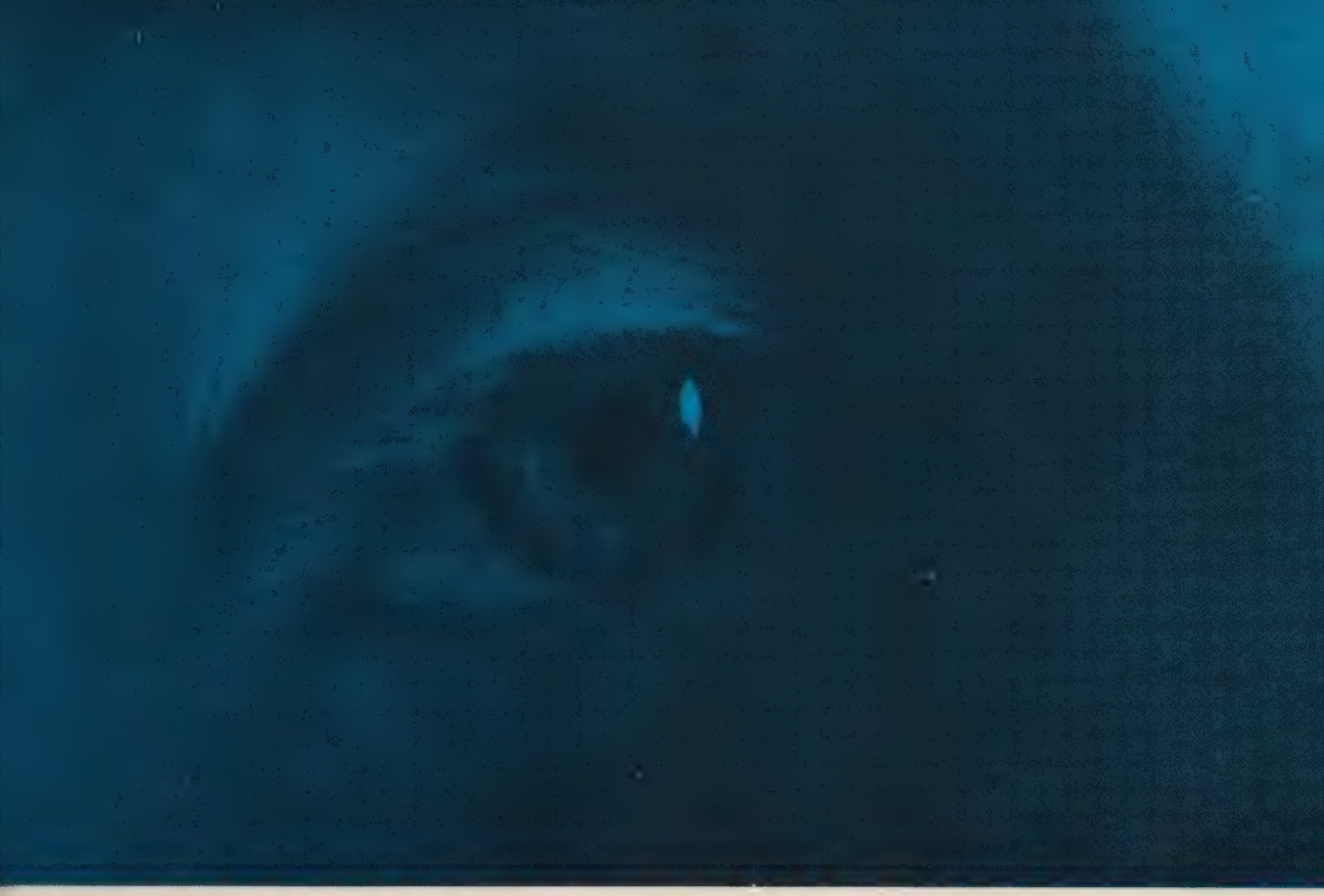
Sudden Cardiac Death

edited by BORYS SURAWICZ *and* E. D. PELLEGRINO, *222 pp., ill., Grune & Stratton, Inc., New York City, 1964. $9.50*

Sudden cardiac death in recent years has become a topic of great importance with the realization that not all such deaths are inevitable. The greatest stimulus to increased study of the many problems associated has been the demonstration that the arrested or fibrillating heart can be assisted in maintenance of its pumping function, occasionally to the point where the heart eventually can resume its vital task. This book is the record of a symposium held at the University of Kentucky in the fall of 1963. The several contributors discussed the various types of cardiac catastrophies: arrest, ventricular fibrillation, heart block, and tachycardias, as well as pulmonary embolism.

Zoll has outlined a program for cardiac arrest which deserves attention. Such arrests, often sudden and unheralded, cannot be treated with any hope of success unless the attending physician has a plan in mind. Zoll advocates a precordial blow with the fist as the first therapeutic step. It is unfortunate that his last step is thoracotomy, since Jude points out in his chapter that closed external massage can effectively maintain circulation. If closed methods fail, and one should allow a reasonable time for the attempt, perhaps an hour, the

(Continued on page 18A)



DEPRESSION AT THE ROOT OF INSOMNIA?

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BOOK REVIEWS

(Continued from page 16A)

chance of success of a following thoracotomy approaches zero.

The book touches briefly upon prophylactic considerations and earlier recognition of cardiac arrest. It is becoming obvious that there are classes of patients who should be considered candidates for cardiac arrest, predominantly those with recent myocardial infarctions. Such a group in some hospitals are segregated in special care units with electronic monitoring systems that can announce the event of arrest by audible and visual signals. Concentration of such patients in special care units with special monitoring systems should result in greater salvage from more prompt recognition of patients with cardiac arrest.

REUBEN BERMAN, M.D.
Minneapolis

Current Psychiatric Therapies—Vol. IV

edited by JULES H. MASSERMAN, *315 pp., ill., Grune & Stratton, New York City, 1964. $9.75*

"Current Psychiatric Therapies—Vol. IV" is part of a series compiled and edited by Dr. Masserman and is, as he predicts, rich in chapters on the rationale and techniques of family, group, and community therapies. The contributors selected write expertly on present-day psychiatric practices or of research findings. These papers establish some principles for mental health program planning that are quite exciting in their boldness and refreshing in their concepts.

Throughout the work is found emphasis that the entire medical profession is responsible for the care and treatment of mental conditions and that more general medical and nonmedical facilities are usable in mental health programs. In keeping with these themes, several papers of special interest to the medical practitioner are noted: "Psychotherapy in General Medical Practice" by Sheeley, "Modern Treatment of Drug Addiction" by Maddux, and "Mileau Therapy" by Artiss. Part II—"Childhood and Adolescence"—deals with the knotty and oft frustrating problems of elective mutism, treatment of psychotic children, therapy with adolescents, and the youthful offender as a patient.

Significantly, for the psychiatric practitioner, whether in private or public practice, "Current Psychiatric Therapies" emphasizes the interest in transitional and social methods of treatment. This breaking away from the traditional gives credence to Dr. Daniel Blains's introduction that there is a new look in modern psychiatric practice. For those at all interested in mental health, this volume is excellent for its readability, for its content, and for its reference value.

RUSSELL O. SAXVIK, M.D.
Bismarck

Hemoglobin, Its Precursors and Metabolites

by F. WILLIAM SUNDERMAN *and* F. WILLIAM SUNDERMAN, JR., *360 pp., ill., J. B. Lippincott Co., Philadelphia, 1964. $16*

This is an excellent book for the individual doing research on hemoglobin: the chemical structure, the precursors, and the various components necessary for breakdown.

Section I discusses the chemical structure of hemoglobin, the measurement of hemoglobin in blood and plasma, and the various methods of determining deriva-

(Continued on Page 20A)

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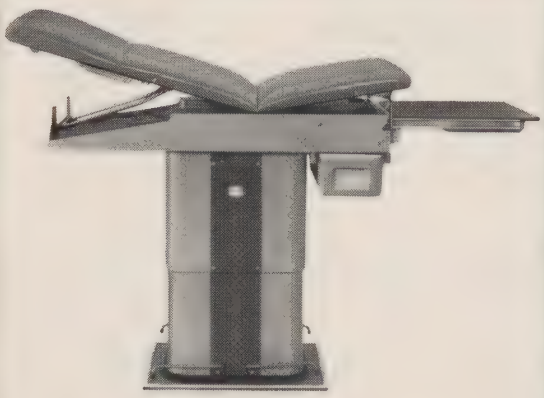
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BOOK REVIEWS

(Continued from page 18A)

tives. The detection of occult blood in the feces and urine, as well as the immunochemical recognition of hemoglobin and myoglobins in the urine, is most important to the clinician and the general practitioner.

The electrophoretic identification of hemoglobins and determinations of the amount of hemoglobin A, as well as the various alkali-resistant hemoglobins for the clinical diagnosis of several diseases, and the genetic and clinical manifestations of the hemoglobinopathies are more important now than they were several years ago.

Section II discusses iron and its relation to tissue utilization, iron-binding capacity of the blood, diseases of iron metabolism, and iron overload such as in hemosiderosis and hemochromatosis.

Section III on porphyrins goes into the measurement of porphyrin and its precursors and conditions of porphyria seen in clinical practice.

Section IV discusses folic acid and vitamin-B deficiency, methods of biologic assay of folic acid, determination of urinary formiminoglutamic acid to determine folic acid deficiency, and diagnosis of B_{12} and folic acid deficiencies that are very important to the clinician today because of the greater increase of pernicious and megablastic anemias.

Section V on bile pigments discusses the hemoglobin in relation to bile pigments, measurement of bilirubin, and fractionation of free and conjugated bilirubins, with the urobilinogen in the urine and in the feces.

The last section, section VI, discusses the erythrocyte production and destruction and erythropoiesis due to erythropoietin, tumors producing erythropoiesis-stimulating factors, determination of the age distribution of erythrocytes, and differential diagnosis of polycythemias and hemolytic anemias. In the past several years many cases of hereditary methemoglobinemia have occurred, and it is important for the clinician to be well aware of this abnormality.

The book has a great deal of information, is well written, and goes into detail regarding many of the pathological problems that are associated with blood and its derivatives. I find it an excellent reference book for anyone's library.

E. N. NELSON, M.D.
Minneapolis

An Atlas of Vascular Rings and Related Malformations of the Aortic Arch System

by JAMES R. STEWART, OWINGS W. KINCAID, *and* JESSE E. EDWARDS, *171 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $10.75*

The authors present a comprehensive "Atlas of Vascular Rings and Related Malformations of the Aortic Arch," combining embryology, pathological anatomy, radiological diagnosis, and clinical and surgical aspects of the various lesions. Classification of the lesions is extensive, and each is documented with numerous detailed illustrations and excellent photographs of pathological specimens and X-rays that contribute significantly to easy reading and understanding. An adequate bibliography is included for the advanced student. The text, as indicated by the publishers, is the first book devoted entirely to this group of malformations and provides a single source of detailed information of interest to every discipline concerned with the diagnosis and treatment of these lesions.

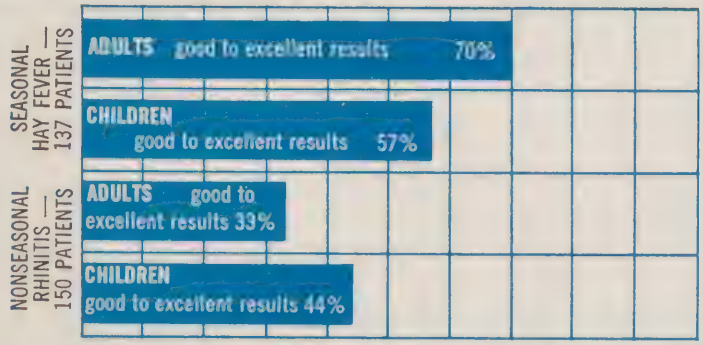
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News Briefs . . .

North Dakota

DR. LEONARD KLASSEN has begun practice in Devils Lake, associating with Drs. James H. Mahoney, Isadore L. Lazareck, and Lemuel T. Longmire, Jr. A 1959 graduate of the University of Alberta Faculty of Medicine, Edmonton, the Canadian native interned at Edmonton General Hospital, took a year of pediatric residency at the University Hospital in Seattle, and has practiced in High Prairie, north of Edmonton.

Minnesota

DR. OWEN H. WANGENSTEEN, professor and chairman of the Department of Surgery at the University of Minnesota Medical School, has been awarded the Alpha Sigma Phi distinguished merit award. Dr. Wangensteen was cited by the social fraternity for his "recognition in the field of abdominal surgery and research, developer of the Wangensteen Pump . . . (and) distinction as a teacher." Dr. Wangensteen received his M.D. and Ph.D. degrees from the university and was named head of the Department of Surgery in 1931.

* * * * *

DR. DON C. PEARSON recently announced plans to leave his practice in Lamberton, following two years in the community. He plans to specialize in ophthalmology in Pennsylvania.

DR. DWIGHT C. MC GOON, a Mayo Clinic heart surgeon, taught open-heart surgery techniques in Bangkok, Thailand, in January, under the auspices of the U.S. State Department. He recently was honored after completing his one hundreth consecutive open-heart operation involving implantation of artificial valves.

* * * * *

DR. RICHARD E. OLSON, after a year of association with the Valley Medical Clinic in Jordan, has joined the clinic partnership with Drs. Gerald E. Nelson and George T. Schimelpfenig of Chaska. A 1960 graduate of the University of Minnesota Medical School, Dr. Olson began practice in Jordan after Army duty. He is a native of Litchfield.

* * * * *

DR. RICHARD L. CASTILLO, a San Francisco internist, has begun practice in Plainview. He received his M.D. degree from the University of California in 1957 and has been in private practice in San Francisco.

* * * * *

DR. RUSSEL G. FOFOFF of Graceville now is practicing part-time at the Valley Clinic, Browns Valley. Opening of the clinic on a half-day schedule was accomplished in January.

* * * * *

TWENTY MINNESOTA DOCTORS have been named fellows or associates of the American College of Physicians. Newly accepted fellows are Dr. Martin E. Janssen, St. Paul, Drs. Mark C. L. Hanson and Herbert F. R. Plass,



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Minneapolis, and Drs. Grant R. Diessner, Francis E. Donoghue, John F. Fairbairn II, Emilio R. Giuliani, Norman G. Hepper, Charles G. Moertel, Richard J. Reitemeier, and Ralph E. Smith, Rochester. Designated as associates are Drs. Wilbert J. Henke, Frank Q. Nuttall, and Alfred F. Anderegg, St. Paul, Drs. James N. Karnegis, and Franklin C. Norman, Minneapolis, and Drs. Peter J. Dyck, Robert A. Kyle, Robert J. Schultz, and John W. Worthington, Jr., Rochester.

° ° ° ° °

DR. ALLEN F. SCHEUNEMAN has discontinued his practice in Warroad and is now associated with the medical staff of the Falls-Starekow Clinic in Thief River Falls. A 1954 graduate of the University of Nebraska College of Medicine, Dr. Scheuneman received postgraduate education in the U.S. Air Force after internship at Immanuel Hospital in Omaha. Dr. Scheuneman, a general practitioner, received special training at the universities of Nebraska and Colorado.

° ° ° ° °

DR. LOUIS FILIATRAULT, a general practitioner, has joined the Coon Rapids Medical Clinic. He formerly was in practice at Silver Bay. Dr. Filiatrault is a graduate of the Stritch School of Medicine of Loyola University, Chicago.

° ° ° ° °

DR. H. WAYNE JOHNSTON has joined the professional staff of the East Range Clinic at Virginia. A graduate of the University of Minnesota Medical School, Dr. Johnston has been in general practice in Virginia for the past twelve years.

° ° ° ° °

DRS. WILLIAM A. BLACK, FRANK J. CARTHEY, and LAWRENCE R. RINGHOFER of the Seifert Clinic are among the first occupants of the recently opened New Ulm Medical Center. The building is owned by the Seifert Clinic, which was founded by the late Dr. O. J. Seifert.

° ° ° ° °

DR. ROBERT B. PIERCE of Mountain Lake has announced plans to join in a partnership at the Heron Lake Clinic with Dr. George R. McNear. Dr. Pierce, a general practitioner, is a graduate of the University of Minnesota Medical School. He interned at Patterson, N.J., and has practiced at Mountain Lake for the past two years.

° ° ° ° °

DR. CARL A. SCHWARTZ, formerly of Austin, is now associated with Drs. William S. Chalgren and Joshua B. Lund in the practice of neurology and psychiatry at Mankato. A graduate of the University of Pennsylvania School of Medicine, Dr. Schwartz is a past fellow of the Mayo Clinic. His professional affiliations include the American Psychiatric Association and the Academy of Psychosomatic Medicine.

Deaths . . .

DR. JOSEPH H. WEISBERG, 63, Superior, Wis., general practitioner, died Jan. 8. Born in Milwaukee, Dr. Weisberg was a graduate of Marquette University School of Medicine. At the time of his death he was chief of staff of St. Mary's Hospital, Superior. He was a member of county, state, and national medical associations, the American Academy of General Practice, the American Diabetes Association, and past president of the Interurban Medical Society.

(Continued on page 24A)



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WANTED: General practitioner or internist to join group of five doctors in Breckenridge, Minnesota, 5000 population. Community from which practice is drawn approximates 15,000. Age—under 35 years. Salary open with opportunity for full partnership later. Excellent 125 bed hospital. New air-conditioned building. Golfing, hunting, fishing available in area. Position open July 1, 1964. Write: Breckenridge Clinic; Breckenridge, Minnesota.

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DOCTOR for general practice work in established clinic with another Doctor. Beginning salary $1500.00 per month with opportunity for partnership after one year. Progressive W. N. Dak. town with 30 bed hospital. Reply Box 25, Journal Lancet.

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DEATHS

(Continued from page 23A)

DR. J. ANTHONY MALERICH, 73, retired South St. Paul physician, died Jan. 16. Born in Arlington, Minn., he was graduated from the University of Minnesota Medical School in 1927. Dr. Malerich was a member of county, state, and national medical associations and the American Academy of General Practice and was an associate fellow of the International College of Surgeons.

* * * * *

DR. JOHN E. POWER, 73, retired Duluth otolaryngologist, died Dec. 18. A native of London, Ont., he was a 1917 graduate of Queen's University Faculty of Medicine, Kingston, Ont. Dr. Power was a past chief of staff of St. Mary's Hospital, Duluth, a member of county and state medical associations, and a fellow of the American College of Surgeons.

* * * * *

DR. DALE D. TURNACLIFF, 76, St. Paul dermatologist, died Dec. 29. He was a graduate of the University of Minnesota Medical School and a member of county, state, and national medical associations and the American Board of Dermatology. A resident of St. Paul for fifty-two years, Dr. Turnacliff was a veteran of World War I and past national president of Phi Beta Pi.

* * * * *

DR. AXEL S. N. NORAN, 77, Edina pediatrician, died Dec. 27. He was born in Fergus Falls and received his M.D. degree from Northwestern University in 1910.

* * * * *

DR. CARL G. BURTON, 70, retired St. Paul physician, died Jan. 18. Born in Sweden, he was graduated from Macalester College, St. Paul, received his M.D. from the University of Minnesota, and interned at Bethesda Lutheran Hospital, St. Paul. A resident of St. Paul since 1914, Dr. Burton was an honorary member of the Mounds Park Hospital staff and a member of county, state, and national medical associations.





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—Martz, B. L., Steinmetz, E. F., and Kraner, J. C.: Studies of a New Diuretic, Cyclothiazide, J. Indiana M.A., 55: 173, 1962.

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APRIL 1965





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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, 22:527, 1964.

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Isoephedrine Hydrochloride..... 60 mg.
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File: Diarrhea

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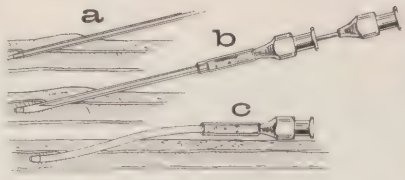
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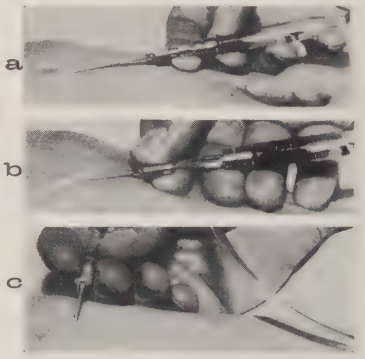
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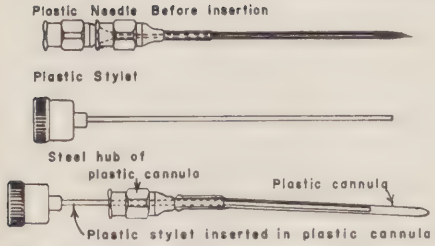




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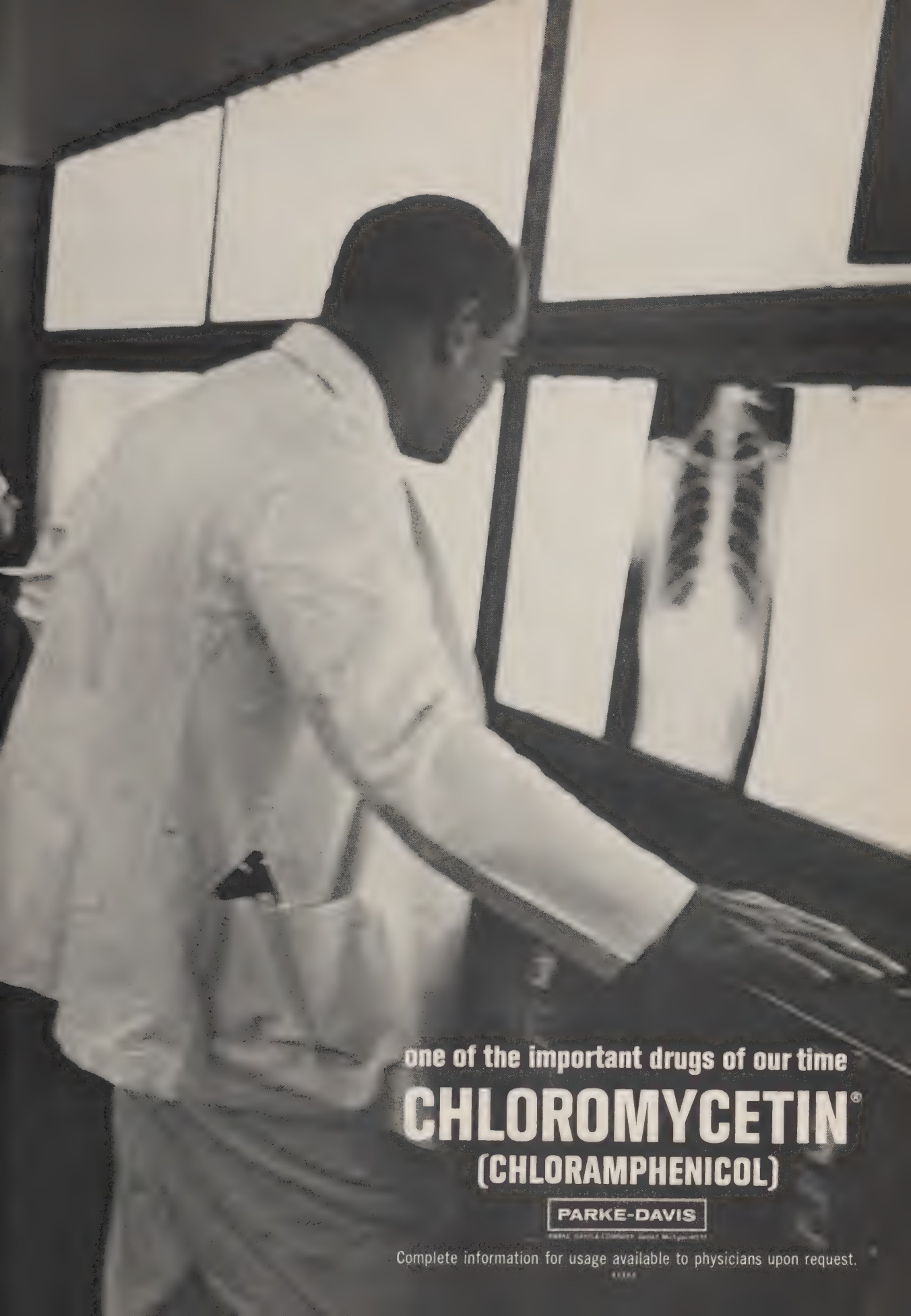
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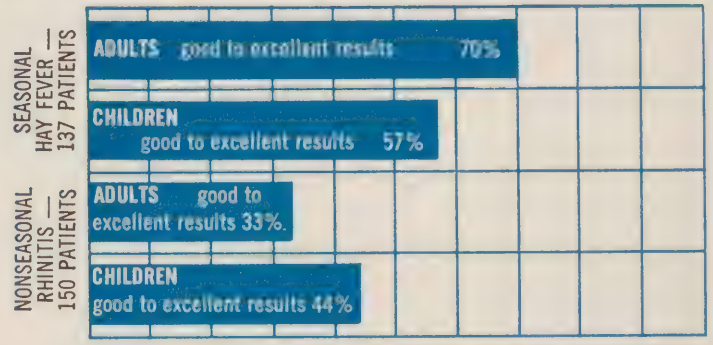

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Cardiovascular disease is the leading cause of death in this country. Many of the deaths are from chronic disease, but others occur because of a sudden, often reversible, change in the patient's cardiovascular status. In the latter case prompt treatment can be lifesaving. "Cardiac Emergencies," by James H. Kelly, M.D., attending physician at the Veterans Administration Hospital in St. Cloud, emphasizes the immediate therapy of such reversible situations. Dr. Kelly's article in the May issue of THE JOURNAL-LANCET inaugurates a series of articles on "Cardiovascular Disease for the Practitioner" that has been arranged for and edited by John F. Briggs, M.D., St. Paul, a clinical professor of medicine at the University of Minnesota Medical School and associate editor of *Geriatrics*.

Another paper relating to the treatment of heart disease is, "The Use of Large Doses of Angiotensin in Acute Myocardial Infarction with Shock," by Martin S. Belle, M.D., and Robert J. Jaffee, M. D., of Miami, Florida. Dr. Belle is with the section on cardiology at the University of Miami, and Dr. Jaffee is on the staff of the Mount Sinai Hospital there.

"Coexistent Sarcoidosis and Gout," by Captain Neil A. Kurtzman of the William Beaumont General Hospital, El Paso, presents a case that indicates sarcoidosis and gout may be more than casually related.

At the Quain and Ramstad Fall Clinical Conference, Hugh B. Lynn, M.D., section of pediatric surgery, Mayo Clinic, pointed out the advantages and disadvantages of a particular surgical treatment for aganglionic megacolon which will be published in the May issue under the title, "Evaluation of the Duhamel Type Operation for Hirschsprung's Disease."

Part III of "The Psychiatry of Presidential Assassination," by Donald W. Hastings, M.D., professor and head, department of psychiatry and neurology, University of Minnesota Medical School, deals with the attempts made upon the lives of Theodore and Franklin D. Roosevelt. Readers of Parts I and II will need no urging.

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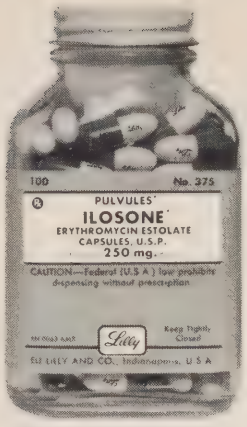
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1. Stoll, L. J.: The Use of Trifluoperazine ['Stelazine'] in General Practice, M. Press 243:578 (June 29) 1960.

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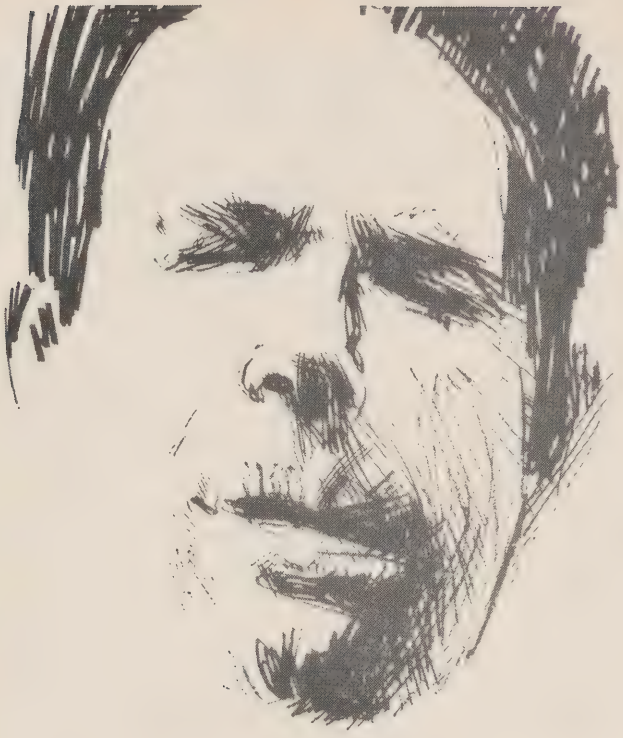
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Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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Quain and Ramstad Fall Clinical Conference

The Pathogenesis and Management of Acne

R. W. FARDAL, M.D.

Bismarck

Acne bears the unfortunate distinction of being one of the most common and poorly understood diseases. It has been estimated that perhaps 90% of adolescents are affected, yet it is not confined to young adults and adolescents since cases are recognized during advanced ages and infancy. Unhappily, much treatment seems to be guided by folklore and time-honored remedies rather than comprehension of physiology and pathology involved.

PILOSEBACEOUS ANATOMY AND PHYSIOLOGY

The prepuberal pilosebaceous follicle undergoes marked hyperplasia with the androgenic stimuli of puberty. It has been recognized since ancient times that eunuchs, that is, prepuberal castrates, do not develop acne although they will develop it after administration of androgens. Sebaceous glands of prepuberal boys and girls enlarge two to three weeks after androgen administration while this has little effect on the adult.[1] Androgens have no effect on postpuberal male sebaceous glands but enlargement occurs in young and postmenopausal women. Physiological quantities of estrogen and progesterone have little effect on the sebaceous gland; no significant variation occurs during the menstrual cycle.[2] Minute doses of exogenous androgens maintain glandular enlargement despite huge doses of estrogens.[1]

R. W. FARDAL *is a dermatologist at the Quain and Ramstad Clinic, Bismarck.*

Follicles occur on all skin surfaces except the palms, soles, and mucocutaneous regions. They are largest and most numerous in the face and scalp, midline of the back, and pubes. Almost all sebaceous glands are appendages of hair follicles but some exit independently. Functional sebaceous glands are present in the fetus. Indeed, the enshrouding vernix caseosa is partly sebaceous secretions.

Sebum is a hydrophilic mixture of lipids and cellular debris. This contains free and esterified fatty acids, cholesterol, and squalene. Kligman[3] emphasizes the fact that sebum is continually produced in a river-like flow propelled by capillary attraction in the stratum corneum or outermost layer of epidermis. Sweat is very important in promoting the rapid spread of the fatty surface film which flows 3.3 cm. per second over moist skin.[4] Removal of this film by ether, alcohol, or other solvents leads to rapid replacement within minutes; subsequent levels may be even greater because of follicular emptying in rebuilding the reservoir. Kligman[5] also maintains that sebum contributes little to the normal skin barrier function and has little or no fungistatic or bacteriostatic activity, as was once believed.

Keratinization of the terminal sweat duct and pilosebaceous follicles may proceed independently of the surface epidermis. These areas seem hypersensitive to both nonspecific irritation and vitamin A; poral occlusion may result.[6,7] The worm-like mite, Demodex folliculorum, is a fre-



Fig. 1. Typical closed comedones and early acne papules of forehead

quent inhabitant of normal follicles but may cause hyperkeratinization.[8]

PATHOLOGY, PHYSIOLOGY, AND MICROBIOLOGY

Strauss[9] has made significant contributions in understanding the pathogenesis of acne. The pilosebaceous follicles demonstrate sebaceous gland hypertrophy and widely dilated canals filled with keratin, lipids, and microorganisms. Fine, short, vellus hairs are usually present. The earliest pathological changes probably occur in this canal, not in the duct as suggested by other investigators. However, the upper follicle is probably hyperactive since it elongates, dilates, and is hyperkeratotic.[10]

Comedones, the basic lesions, are of two types. The "blackhead" or open comedone is an epithelium-lined sac filled with horny lamellated material and rarely becomes inflammed. The "whitehead" or closed comedone (Fig. 1) is the "time bomb" since subsequent rupture of the extended follicular walls excites a foreign body inflammatory response in the adjacent dermis. Investigation has confirmed that sebum, keratin, and follicular bacteria will produce inflammation on intradermal injection, resulting in inflammatory papules, pustules, nodules, and cystic lesions.

Superficial pustules may occur in follicles without comedones or in closed comedones when small breaks in the follicular walls allow sebum to escape into the dermis.

Healing ultimately occurs by hypertrophic or atrophic fibrosis. The inflammatory reaction may also be encapsulated by new epithelial proliferation from the follicular wall remnants.

The precise role of endocrine hormones in the pathogenesis of acne is unknown; this is not surprising, considering the lack of information relating these factors to more basic processes such as keratinization. Excessive adrenocorticosteroids produce papular acneform eruptions which lack comedones and are relatively independent of steroid level and age of the patient.

Several investigators suggest that pilomotion is a factor since fine, lanugo-like vellus hairs may be unable to maintain patency of the pilosebaceous unit, making it easier for sebum and keratin to occlude such a follicle. However, in bearded areas bearing coarse, terminal hairs, there may be 2 channels in the follicle neck, 1 bearing the hair and the other connecting the sebaceous duct. Van Scott and MacCardle[11] reported that the state of the hair has little influence on follicular patency while hyperkeratinization of the sebaceous channel is basic.

Chloracne is due to topical application of chlorinated hydrocarbons and occurs most frequently in petrochemical workers and machinists using cutting oils. Shelley and Kligman[12] made extensive studies of responses to the application of chlornaphthalenes. They found that follicular hyperkeratosis became apparent in one to three weeks and sebaceous atrophy in three to four weeks. Comedones formed in four to six weeks, followed by pustules, nodules, and abscesses. Inflammation was initially perifollicular and intrafollicular but destruction of the follicular wall did introduce follicular contents into the dermis with subsequent abscess formation. Lesions continued to form for several months after daily application of halogenated hydrocarbon (Halowax 1014®) for five weeks.

Bacterial cultures of inflammatory lesions most commonly reveal Corynebacterium acnes or Micrococcus (staphylococcus) albus; Micrococcus pyogenes is less common and yeasts are rare. At times, cultures may reveal no organisms, lending support to the concept of a primary irritant effect from released follicular contents. The bacillus, C. acnes, is a microaerophilic gram-positive rod. C. acnes injected into sterile, quiescent keratinous cysts converts these into inflammatory lesions through rupture of the wall.[13] In vitro studies revealed C. acnes sensitive to penicillin, erythromycin, tetracyclines, chloramphenicol, and novobiocin but insensitive to streptomycin, neomycin, and sulfa.[14,15] Generally similar results are obtained with micrococci. However, there is no direct correlation between results of these in vitro tests and clinical response to the antibiotics.

THE MANAGEMENT OF ACNE: FACT AND FANCY

The patients' understanding is confused by folklore, rumor, and the blatant admonishments of cosmetic concerns that each proprietary agent is the "sure cure" to physiological and psychological problems of the disease. It is the rare patient who has not employed several proprietary medications prior to seeking medical consultation. The physician must meet this challenge by advising the patient and not employing blandish-

ments such as "He'll outgrow it," "Lots of young people have this problem," "Wash frequently."

A fourfold approach to local and systemic therapy may be summarized as follows:

1. Reduce excessive keratin and debris in pilosebaceous follicles and ducts.

2. Reduce and prevent inflammation involving the pilosebaceous unit and adjacent tissues.

3. Avoid irritating external factors such as manipulation of lesions or occlusive cosmetics.

4. Avoid internal acnegenic factors such as halogens, foods, and emotional stress.

THE REDUCTION OF FOLLICULAR PLUGGING

Cleanliness is of little importance to the average patient. Acne cannot be scrubbed away; indeed, there is some indication that too vigorous or frequent washing may accentuate acne through edema, hyperemia, and follicular rupture.

The various commercial soaps and detergents, with or without added bacteriostatic agents, are adequate in mild acne. Heavily perfumed or superfatted toilet soaps seem less effective. Severe acne generally requires medicated cleansing agents, most of which employ sulfur, salicylic acid, and hexachlorophene in a cream or bar form. Well known varieties are Fostex®, Acnaveen®, and Acne-Dome®. Brasivol® is an agent containing abrasive particles of aluminum oxide.

Since sebum contributes little to follicular occlusion and is rapidly replaced after depletion, degreasing agents are of little value.

Keratolytic or peeling and drying agents are widely employed in colorless or colored preparations. Most contain sulfur, resorcin, salicylic acid, or sodium thiosulphate in various concentrations and combinations. Hot sulfurated lime solution is an efficient keratolytic agent. A bit of showmanship is added by employing carbon dioxide "slush" composed of pulverized solid carbon dioxide, acetone, and sulfur. Topical steroids are sometimes added to keratolytic agents to relieve irritation or excessive dryness.

Physicians must realize that all cleansing agents are more valuable to prophylaxis than to elimination of existing lesions. Open and closed comedones may show some response but deeper inflammatory lesions seldom react significantly.

Acne surgery, the manual removal of open and closed comedones, papules, and superficial pustules, remains one of the physician's most neglected duties to the patient. Both the Schamberg and Lawton comedone extractors (Fig. 2) may be used; the former is less traumatic and safer for patient use. Larger, inflammatory lesions should, however, not be treated.



Fig. 2. Comedone expressors: Lawton (top) and Schamberg (bottom) types

THE REDUCTION OF INFLAMMATION

Irradiation purportedly reduces inflammation. Ionizing X-ray emissions apparently have some antiinflammatory action and also diminish follicular keratinization, yet the major anatomic and physiologic alteration produced is temporary sebaceous gland atrophy. A common program employs 75 r weekly for six weeks. The program may be repeated but total skin dosage should not exceed 900 to 1,300 r to any area.

Erythema doses of natural or artificial ultraviolet irradiation apparently reduce inflammation and follicular occlusion. Tanning exposures without the production of erythema are less useful.

Systemic administration of antibiotics and sulfonamides has contributed significantly to acne management. The exact mode of action is unknown but may be due to the reduction of inflammation rather than alteration of bacterial flora of the skin or intestines.

Double-blind studies employing various antibiotics, sulfonamides, and sulfones have, with few exceptions, demonstrated beneficial results.[16–19] Such drug therapy does not appear to alter bacteriological characteristics of lesions during or after treatment.[14] Clinically, the various tetracycline derivatives seem to be more effective. Dosage schedules vary but treatment is usually initiated with 250 mg. four times daily with gradual reduction over a period of a few weeks to the smallest practical maintainance dose, generally 250 to 500 mg. daily. Cornbleet[20] reported a remarkable incidence of improvement in patients treated with tetracycline without local measures. Prolonged therapy is common, practical, and remarkably free of untoward reactions.

Corticosteroids are unique in their ability to produce papular eruptions as well as depress inflammatory response in existing acne. Parenteral or oral corticosteroids are rarely justified but intralesional injection into nodules and cysts is common. Triamcinolone diacetate is usually employed in concentrations of 2.5 to 10 mg. per ml. Corticosteroid creams are also utilized fol-

lowing the application of warm, moist compresses.

THE AVOIDANCE OF EXTERNAL IRRITANTS

The patient should avoid self-manipulation of lesions. Too vigorous massage, washing or use of commercial complexion brushes, or rubbing with the hands or woolen garments may rupture distended follicles or produce edema.

Most cosmetic makeups are occlusive and will accentuate acne. Heavy use of hairsprays has a similar effect. So-called "medicated" makeups are less occlusive, but there is a natural tendency for the patient to rely on such covering agents while neglecting active therapy.

Exposure to halogenated hydrocarbons is limited to industrial workers.

THE AVOIDANCE OF INTERNAL IRRITANTS

The ingestion of iodine in the diet, water, or drugs apparently has little influence unless taken to excess. Halogens, however, are follicular irritants systemically as well as topically. Most dermatologists feel that the follicular irritant effect of chocolate, sharp cheeses, saltwater fish, crustaceans, and mollusks warrants avoidance of these items. In my opinion, other dietary items are seldom significant.

Abnormal carbohydrate metabolism is suggested by the fact that resistant lesions may respond to oral antidiabetic drugs or intralesional insulin.[21,22] Tolbutamide (Orinase®), chlorpropamide (Diabinese®), and phenformin hydrochloride (DBI®) have been administered orally. The latter does not lower the blood glucose in nondiabetic patients but increases cellular glycolysis.

Adrenal and gonadal steroids contribute to acne but their effect is poorly understood. More is known about their effect on sebaceous glands. Testosterone and progesterone have quite similar structures. It has been suggested that premenstrual exacerbations were due to progesterone. Some investigators have employed estrogen therapy during the progestational phase of the menstrual cycle;[23] the synthetic progestational steroids, commonly used to supress ovulation, have had wider use with fewer objectionable side effects and most effectively in women who experience premenstrual flares of acne.

The role of emotional factors is difficult to evaluate; use of psychotherapy and psychotherapeutic drugs has added little to management.

SUMMARY

Acne occurs secondary to occlusion of the pilosebaceous follicles. Inflammatory lesions result from follicular rupture with release of irritating sebum, keratin, and bacteria into the adjacent tissues.

Therapy must reduce follicular occlusion; this can be done with various keratolytic agents or by manual extraction. Inflammation can be reduced by irradiation, antibiotics, and corticosteroids. The patient must avoid occlusive cosmetics and manipulation of lesions. The action of various endocrine factors is not well understood and emotional factors are difficult to evaluate.

Read at the Quain and Ramstad Fall Clinical Conference, Bismarck, North Dakota, November 7, 1964.

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Erythema Nodosum

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ERYTHEMA NODOSUM is not a disease. It is a syndrome with a characteristic skin lesion which may be associated with a variety of etiologic agents. The characteristic skin lesions are hot, tender, red, oval patches of inflammation up to four inches in diameter with an elevated center usually appearing as crops of symmetrical lesions on the shins but often involving the calves, knees, and buttocks and occasionally occurring on the arms or neck. In a few days they become purplish and livid, then fade to yellow and green and look like an ordinary bruise, and gradually disappear. They frequently become soft in the center and appear fluctuant but never drain. Within three to six weeks the skin lesions disappear.

Characteristically it is acute in onset and accompanied by fever, malaise, and joint pains. The sedimentation rate is usually elevated. It occurs more commonly in women with a sex incidence reported as 3 to 1 or 4 to 1. It is most common during the childbearing years and is often associated with pregnancy or lactation.

Reported series vary in etiologic agents. There are few recent reports in the American literature but more interest in the British and Scandinavian literature. It is generally agreed, however, that erythema nodosum is the clinical manifestation of a hypersensitivity state brought about by a particular agent to which the individual patient reacts to produce the clinical picture. It may be associated with coccidiomycosis, histoplasmosis, tuberculosis, leprosy, lymphogranuloma venereum, ulcerative colitis, appendicitis, cholecystitis, bronchiectasis, meningitis, drug sensitivity (bromides, iodides, or sulfa), or carcinoma. All reported series include many cases of unproved etiology.

The most common etiologic agents reported are (1) tuberculosis, (2) sarcoidosis, and (3) streptococcal infections. Until about twenty years ago, tuberculosis was the most common reported etiologic factor.

Vasey and Williamson[1] reported in 1959 on 70 patients seen over a seven-year period in southern England. They found 45.6% had streptococcal etiology, 35.7% had accompanying sarcoidosis, 5.6% had tuberculosis, and 13% had unknown etiology.

Gordon,[2] in 1961, reported on 115 patients in Liverpool. Twenty percent developed tuberculosis, 7.8% were probably streptococcal in origin, 13% showed bilateral hilar enlargement, and 47% showed no disease apart from the skin lesions.

Johnson, Hanson, and Good,[3] in 1948, reviewed 100 patients with erythema nodosum at the Mayo Clinic and found 4 with tuberculosis, 26 with unspecified upper respiratory infection, 3 with possible sarcoidosis, and 30 without associated disease; the rest had miscellaneous conditions. Nine patients had associated bilateral hilar lymphadenopathy. No disease process other than erythema nodosum was found which might have caused the hilar adenopathy. In 4 of 5 patients followed up, the adenopathy subsided spontaneously. The authors felt that hilar enlargement was of nonspecific etiology and its disappearance could be anticipated as the erythema nodosum subsided.

Bilateral hilar adenopathy associated with erythema nodosum has been referred to more frequently in the past ten years. The largest series was reported in 1952 by Lofgren and Lundbach[4] from St. Gorans Hospital in Sweden. Two hundred and twelve cases of "bilateral hilar lymphoma syndrome" were reported. The syndrome was defined as large, comparatively symmetrical hilar lymphomas and a negative to moderately positive tuberculin reaction. Of these 212 cases, 107 women and 6 men, 113 had associated erythema nodosum. In 30% of the women, it occurred during pregnancy or lactation. None of these patients were less than 20 years old and

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most occurred in the 25 to 39 age group. Sarcoidosis was diagnosed by histopathologic examination in 26.4% of the patients; primary tuberculosis was excluded in all but one patient. The authors concluded that the bilateral hilar lymphoma syndrome is essentially independent of tuberculosis. They proposed that it was instead the primary stage of pulmonary sarcoidosis.

However, Lofgren,[4] in 1946, in studying unilateral hilar lymphadenopathy with associated erythema nodosum, considered tuberculosis to be the etiologic agent in 86% of 102 cases.

Geraint-James,[5] in 1956, reporting on 27 patients with erythema nodosum with bilateral hilar lymphadenopathy, demonstrated sarcoidosis in 24 patients by a positive Kviem test or by direct biopsy. The bilateral hilar lymphadenopathy always resolved spontaneously.

Of Gordon's 15 patients with bilateral hilar adenopathy, only 1 was considered to have sarcoidosis. He suggested that all cases of erythema nodosum be followed by chest X-ray and that their close contacts be investigated for latent tuberculosis.

Vasey and Williamson had 25 patients with bilateral hilar adenopathy in their report of 70 patients with erythema nodosum. They accept the view that this syndrome represents an early stage of sarcoidosis, but they divided these patients into 2 groups on the basis of clinical features and course. All of the patients had fatigue and joint pains. Iritis or conjunctivitis was present in 4 persons. Both groups had an elevated sedimentation rate initially. The majority had a progressive return to a normal sedimentation rate over a period of about sixteen weeks, paralleling the clinical improvement. The symptoms and chest findings cleared in twelve to eighteen months in most. In 5 patients, however, after an initial drop, the sedimentation rate rose again at the eighth to tenth week after onset and persisted at a high level for several months. These patients had a more severe course characterized by dyspnea, cough, and considerable disability. In addition to hilar adenopathy, these patients had parenchymatous changes in the lungs which persisted from seven months to over three years. The secondary rise in sedimentation rate is considered to be of prognostic significance.

Edwards,[6] in 1961, reported 3 patients with hilar lymph node enlargement and erythema nodosum seen in Edmonton, Alberta. They all had a history of recent pharyngitis and elevated antistreptolysin O titers. He feels that his patients represent an early and benign form of sarcoidosis with spontaneous resolution.

DISCUSSION, MANAGEMENT AND PROGNOSIS

Erythema nodosum, thus, is a syndrome in which various etiologic agents may or may not be found. A patient presenting with erythema nodosum should receive a careful diagnostic work-up including throat culture for streptococci, chest X-ray, ASO titers, serial sedimentation rates, tuberculin, and possibly Kviem tests.

If the patient has no abnormalities of the chest X-ray, treatment should be confined to bed rest and salicylates, and one may anticipate that the patient will be up and healthy in four to eight weeks. The patient should probably be followed with tuberculin tests for two years, but at the present time most of these cases are probably due to streptococcal hypersensitivity or idiopathic. Steroids do not affect the general evolution of erythema nodosum. If they are stopped prematurely, the disease will recur and proceed unaltered in character.

If the patient has unilateral hilar adenopathy, primary tuberculosis is probably associated. Steroids should not be used, and the patient should be evaluated and treated as a case of primary tuberculosis.

If the patient has bilateral hilar adenopathy, the consensus of the literature is that the patient has sarcoidosis. No reports of malignant lymphomas were present in the literature reviewed. Serum albumin and globulin determinations, Kviem test, and scalene node biopsy may be done. If there is no parenchymal lung involvement or other clinical signs of sarcoid, one can expect that the patient will be clinically well in six to eight weeks and that the chest X-ray will be normal within six months in most cases and in two years in almost all cases. Treatment again is bed rest and salicylates. The sedimentation rate should be followed serially. If it shows a secondary rise after six to eight weeks, this may indicate a more severe and prolonged course with a more generalized spread of sarcoidosis.

If the patient has bilateral hilar adenopathy and pulmonary parenchymal involvement, the patient has sarcoidosis and may be expected to have a more prolonged course with more disability. In addition to a basic program of rest, steroids may be necessary to help the patient through the more disabling periods of the disease. However, they do not alter the basic course. Most of these patients will improve, but it is also thought possible to have a progressive unremitting course leading to pulmonary fibrosis, cor pulmonale, and death, although no such cases were reported in association with erythema nodosum.

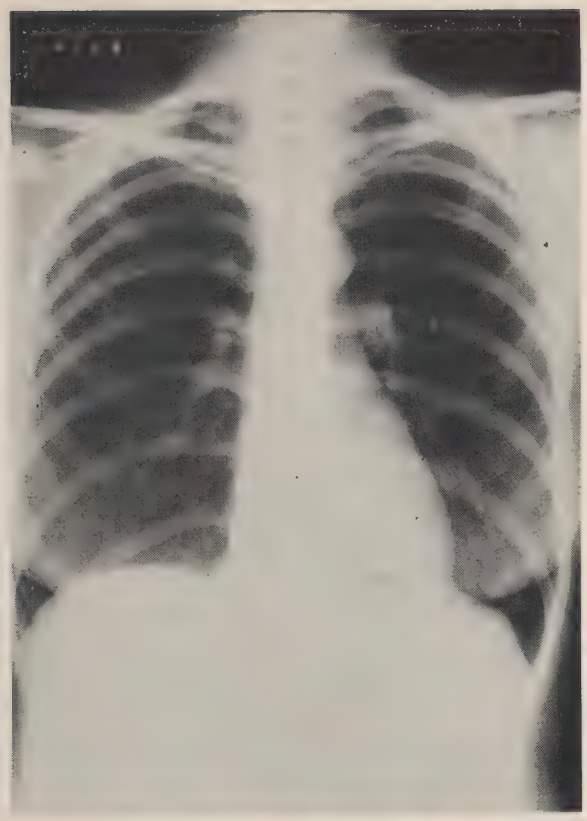


Fig. 1. Case 1. May 20, 1963

CASE REPORTS

Case 1. A 43-year-old nurse was seen at the office on May 10, 1963, complaining of a 3 x 4 inch indurated, tender, hot, red lesion of the left pretibial area which was first noted about one week previously. Except for the skin lesion, she had no complaints. She gave a history of a severe upper respiratory infection with a slight sore throat, severe aching, and a temperature of 101° F. about two weeks before. Physical examination was normal except for the skin lesion. Temperature was 98.8° F., white blood count 2,500, sedimentation rate 40, and differential was normal. She was given an injection of penicillin; salicylates and rest were advised. Chest X-ray was normal. Pelvic and pap smear were normal. During the next six weeks, the lesion gradually subsided and disappeared completely. The patient complained of marked fatigue from the second to the fourth week, but this also improved. The sedimentation rate remained moderately elevated for four weeks and then returned to normal.

This patient represents the course of simple uncomplicated erythema nodosum, probably due to streptococcal infection prior to the visit.

Case 2. A 35-year-old housewife came to the office on March 24, 1962. She stated that two or three weeks previously, she had started with aching of both legs, increased fatigue, and poor appetite. On March 17, 1962, she had noted tender inflamed lesions of both right and left pretibial areas, and soreness and swelling of the right ankle. Past history was not remarkable. There were 5 normal pregnancies and deliveries, the most recent in 1960. There was no history of recent respiratory infection. Physical examination was normal except for mod-

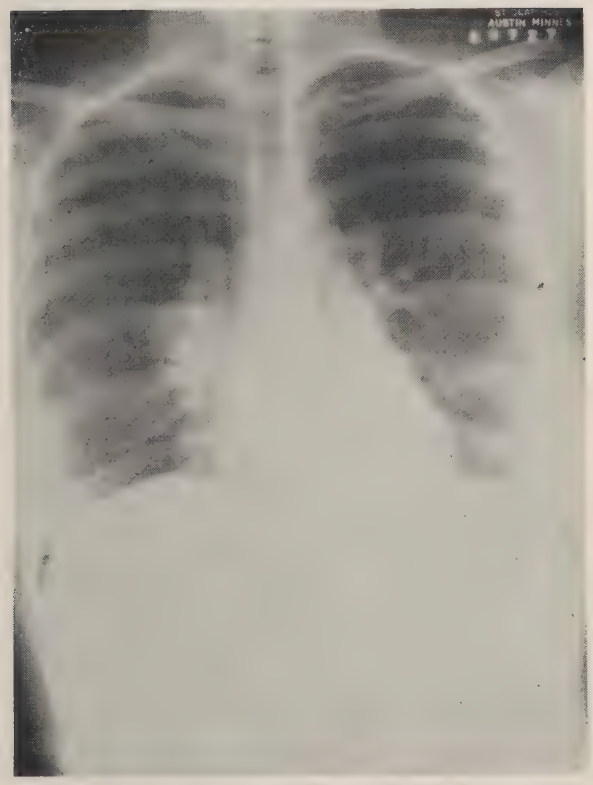


Fig. 2. Case 2. April 6, 1962



Fig. 3. Case 2. Oct. 17, 1962

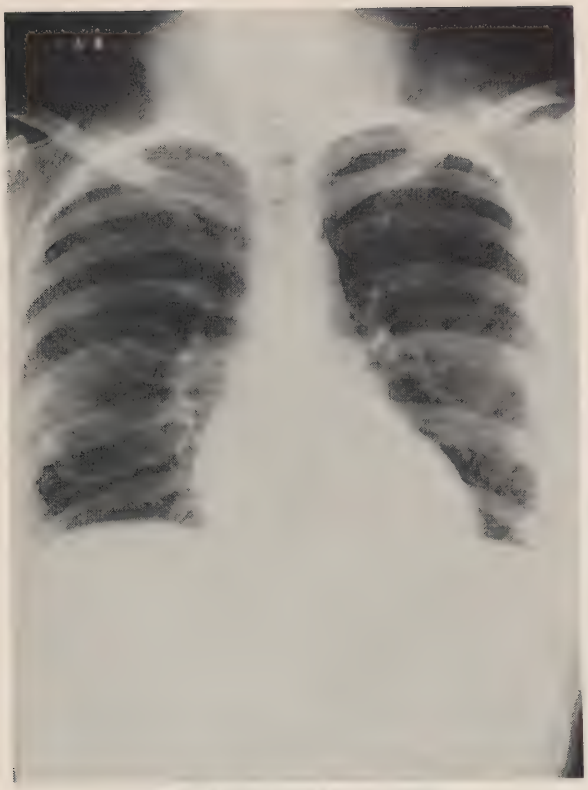


Fig. 4. Case 2. Nov. 5, 1963



Fig. 5. Case 3. Sept. 12, 1962

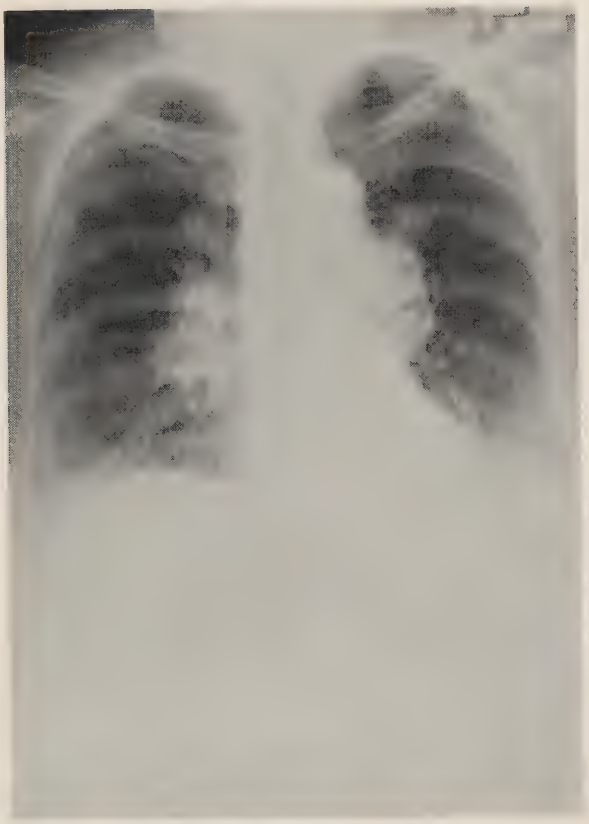


Fig. 6. Case 3. April 1, 1963

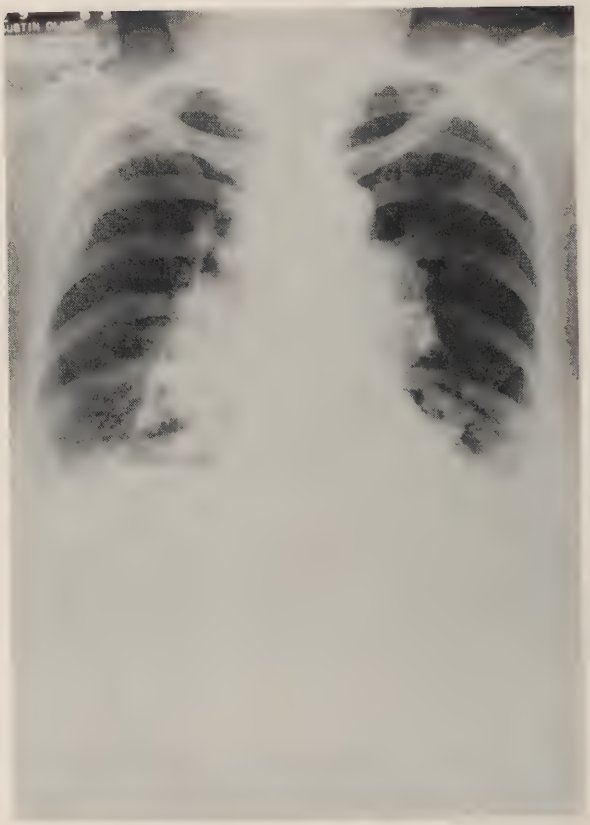


Fig. 7. Case 3. May 29, 1963

erate tenderness deep in the right flank and the changes in the lower extremities. There was 3+ edema of the right ankle and 1+ edema of the left ankle. Both ankle joints were moderately tender. There were areas of induration and inflammation in the right and left pretibial areas which were very tender to touch. Laboratory studies revealed a hemoglobin of 13, a white blood count of 8,100, a sedimentation rate of 67, and a normal differential. Urinalysis showed a 1+ albumin, and there was a normal pap smear. The patient was placed on aspirin and rest at home but failed to improve and was hospitalized on April 5, 1962, approximately four weeks after onset of symptoms.

At the time of admission, the patient had both old and new lesions of erythema nodosum on both legs and the right knee. She had lost 7 lb. since the onset of the illness and complained of moderate fatigue. Her temperature during hospitalization ranged from normal to 100.8° F.

Sedimentation rate was 106 mm. in one hour, serum albumin was 3.9 gm. percent, globulin was 2.9 gm. percent, albumin-globulin ratio was 1.34:1, and calcium was 4.6. Antistreptolysin O titer 333 on April 6 and again on April 13. Throat culture was negative for beta streptococcus and lupus erythematosus prep was negative. Serology was negative. Catherized U/A showed 1+ albumin with normal microscopic. Culture grew a pure aerobacter aerogenes.

Chest X-ray revealed a soft tissue mass of the right hilus which had not been present on a previous chest survey film on May 17, 1960. There was no change in the mass during hospitalization.

Intradermal skin tests for tuberculosis, coccidiomycosis, histoplasmosis, and blastomycosis were all negative. A scalene node biopsy was scheduled but the skin lesions began to improve and it was not done. The patient was discharged on April 14, 1962. The skin lesions disappeared in about a week and the patient felt fine. She did not return again until Oct. 17, 1962. She had a slight upper respiratory infection and a chest X-ray was interpreted as some infiltration in the right lower lung with enlargement of the right hilar shadow. Chest X-ray November 5, 1963, showed a normal right hilar shadow.

This case, despite the unilateral hilar enlargement, probably represents a case of erythema nodosum with hilar adenopathy not due to tuberculosis.

Case 3. A 55-year-old woman on March 7, 1963, began experiencing swelling of the ankles and aching hands and feet. One week later she started with an indurated lesion of the right pretibial area. Sedimentation rate was 66, and she was placed on salicylates and rest at home. There was mild improvement during the first two weeks, but then new lesions appeared on the legs, and the patient developed a nonproductive cough, low grade fever, chest aching, and marked fatigue. Chest X-ray showed marked bilateral hilar adenopathy and moderately heavy diffuse fibrotic infiltration of the pulmonary parenchyma. Previous films on Dec. 26, 1962, and Sept. 12, 1962, had been negative. The patient was admitted to the hospital on March 27, 1963.

Significant past history included a vaginal hysterectomy in 1952, cholecystectomy in 1955 with choledochostomy twice in 1960 for common duct stones, and a bleeding duodenal ulcer in 1962. The patient's mother had died of tuberculosis and the patient had a known positive Mantoux test.

Physical examination on admission revealed marked

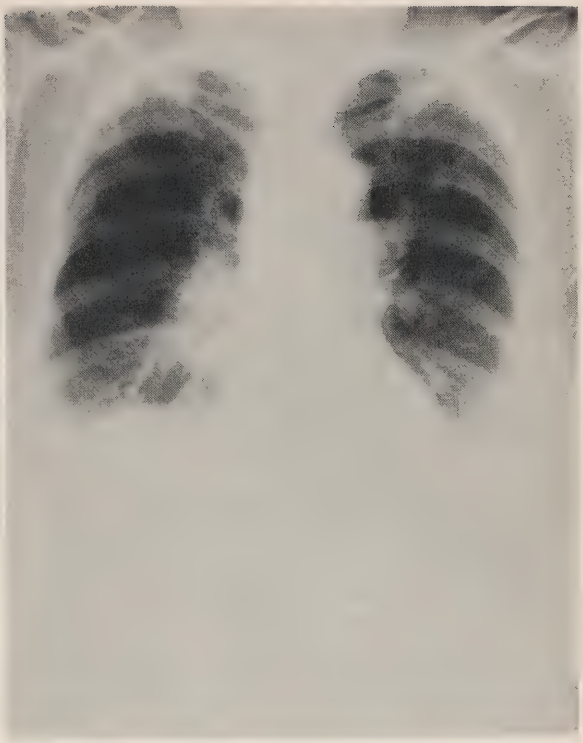


Fig. 8. Case 3. Oct. 28, 1963

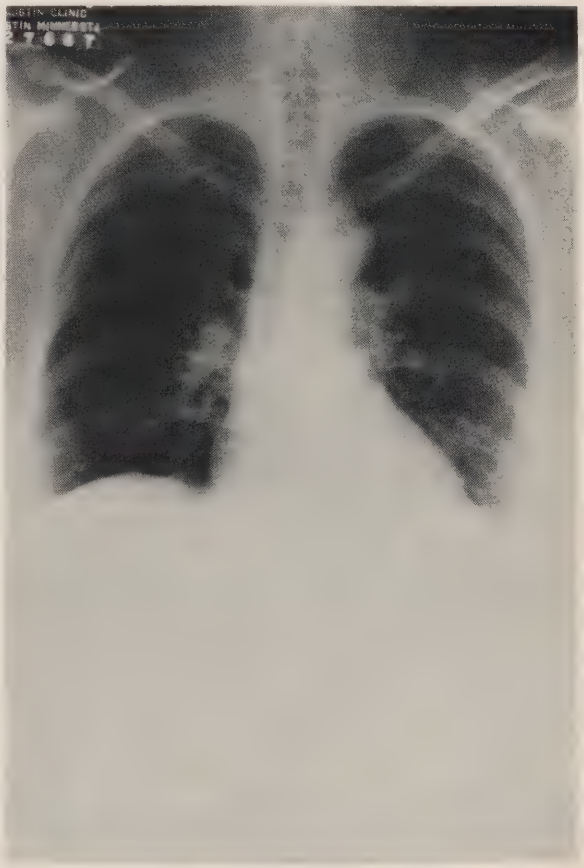


Fig. 9. Case 3. March 5, 1964

right conjunctival inflammation, occasional crackling rales of both posterior lung fields, and typical lesions of erythema nodosum of both pretibial areas. Throat and sputum cultures were negative. Fungus skin tests were negative. Left scalene node biopsy was negative on April 4, 1963. On admission the patient was dyspneic on exertion. One week later she was also dyspneic at rest. The skin lesions gradually subsided during the next two weeks. The conjunctivitis subsided in about four weeks. Dyspnea at rest improved, but dyspnea on even slight exertion persisted even after she was discharged on April 14, 1963, to continue rest at home. The sedimentation rate was initially 66 mm. in one hour. It gradually subsided and on April 19 was 16 mm. in one hour. However, on May 15 it was 37 mm. in one hour, showing a secondary rise six to eight weeks after onset of illness. At the end of May, three months after onset, the patient still had dyspnea on mild exertion, no change in the chest X-ray, and an additional symptom of moderately severe lumbar back pain. Consultation was obtained and the patient was hospitalized from May 31, 1963, to June 12, 1963. A right scalene node biopsy on June 7 was reported to show a noncaseous granuloma and the diagnosis of Boeck's sarcoid made. Steroids were not used because of the patient's recent history of bleeding duodenal ulcer.

The patient continued with rest at home; her strength began to improve and the dyspnea began to subside in July. In September she had improved to the point of feeling well and carrying out her normal activities without fatigue or dyspnea. A chest X-ray on Oct. 28, 1963, showed considerable subsidence of the hilar adenopathy and the pulmonary infiltration. Chest X-ray March 5, 1964, was reported as, "Further decrease in the size of the hilar areas which are now essentially normal in appearance. Minimal residual reticulo nodular pulmonary fibrosis of a diffuse nature along with minimal pleural thickening in the left costophrenic angle."

This case demonstrates erythema nodosum with marked bilateral hilar adenopathy and pulmonary parenchymal infiltration, with marked disability persisting for six months, proved by biopsy to be Boeck's sarcoid. Of interest is the conjunctivitis, the secondary rise of the sedimentation rate, and the fact that the patient improved without use of steroids.

SUMMARY

Recent literature regarding erythema nodosum is reviewed[1–8] and an attempt is made to classify the clinical picture and prognosis according to the findings of chest X-ray. Three illustrative cases are presented.

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ANNUAL CHEST roentgenograms or photofluorograms for asymptomatic persons appear to be economically impractical for detection of lung cancer because the detection rate is so low. During a fifteen-year period, 53,776 examinations were made of 12,174 asymptomatic persons 45 years of age or older. Primary cancers were found in only 10 patients; 9 of them lived no longer than three years after diagnosis, and the tenth received palliative therapy for recurrent cancer. The cost equivalent in terms of time and materials for each cancer detected was $26,890.

VICTOR A. GILBERTSEN, M.D., University of Minnesota, Minneapolis. X-ray examination of the chest. J. Amer. med. Ass. 188:1082-1083, 1964.

Upper Gastrointestinal Hemorrhage in a Community Hospital

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THIS STUDY was prompted by the feeling that it would be necessary to reach a decision as to the practicability for our hospital to institute the use of gastric hypothermia in treatment of the peptic ulcer diathesis. A few years ago there was much enthusiasm for treating upper gastrointestinal hemorrhage by cooling and treating duodenal ulcers by freezing. Hundreds of machines were sold for this purpose. We gave serious thought to obtaining equipment and establishing a team to undertake this treatment but decided that we had better evaluate our experience and decide how often we would actually use this method.

For this reason, cases with upper gastrointestinal bleeding admitted to St. Luke's Hospital, Fargo, N.D., during the years 1959 to 1963 inclusive, were reviewed. St. Luke's Hospital is a 240-bed community hospital in a metropolitan area of approximately 80,000 people.

ANALYSIS OF MATERIAL

In the five years under study, 300 patients were treated on 365 separate admissions to the hospital. Nearly all were adults and in most instances were admitted to the medical service. Three hundred and sixty-five admissions would represent just under 4% of the total number of medical admissions during this period of five years.

Age. The ages of the patients span all decades with the maximum number in the seventh decade. See table 1.

Sex. Two hundred and twenty patients, or 73%, were male; 80 patients, or 27%, were female.

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Twenty-one of the patients died during their hospital stay. This represents 5.4%.

Fifty-eight of the patients underwent surgery.

Seventy-nine patients were admitted a total of 83 times and classified as massive bleeders.

Table 2 indicates the bleeding sites given in the final discharge diagnosis based on clinical, surgical, or autopsy findings.

MASSIVE BLEEDERS

Massive bleeding is not easily defined, and much confusion exists in the literature because reported series are not comparable. In this study it was defined as follows:

1. Active bleeding
2. One or more of the following:
   a. shock
   b. hemoglobin, 7 gm. or less
   c. hematocrit, 25 vols. percent or less
   d. six units of blood used in twenty-four hours

TABLE 1
AGE OF PATIENTS IN STUDY

Decade	*No.*
0- 9	1
10-19	5
20-29	23
30-39	18
40-49	55
50-59	70
60-69	95
70-79	54
80-89	34
90-99	10
TOTAL	365

Actually, the only accurate way to define massive bleeding is to determine blood volume or circulating red-cell mass. It is recognized that hemoglobin and hematocrit readings may be grossly inaccurate especially immediately after hemorrhage. Preexisting anemia and state of hydration further alter these values. Determination of blood volume by the Evans blue method is cumbersome, and it is hoped that newer methods using radioactive isotopes will permit accurate and easily repeated determinations.

DISCUSSION

Bleeding is one of the most challenging manifestations of gastrointestinal disease. It is serious in its own right, signifying organic disease. It cannot be ignored and demands early detection as to site of origin. In a study[1] of vital statistics in Minnesota in 1952, it was found that acute massive hemorrhage was responsible for 46% of deaths reported due to peptic ulcer. It should be pointed out that a person can bleed to death within the gastrointestinal tract without any external show of blood.

Palmer[2] has emphasized the need for a "vigorous diagnostic approach" which calls for esophagoscopic, gastroscopic, and radiological examinations as soon as the patient comes under medical surveillance. He feels that control of severe upper gastrointestinal bleeding is possible only if we know the bleeding site. However, he states there are 3 major deterrents to accurate clinical diagnosis: (1) tendency to play statistics and assume due to ulcer, (2) tendency to assume present bleeding is due to known existing lesion, and (3) delay in examining patient. Such lesions as erosive esophagitis and erosive gastritis won't be recognized unless detected early.

On the other hand, Bockus[3] feels that individualization, with regard to the use of special diagnostic procedures and mature judgment strengthened by consultation, would seem to be preferable to blind and sometimes rigid routines of investigation. In this series, emergency endoscopic procedures were not used. However, radiological investigations during the acute bleeding phase were frequently made.

A patient admitted with upper gastrointestinal bleeding is followed closely by both an internist and a surgeon. Most patients respond to medical treatment which includes the following: (1) studies to rule out blood dyscrasia, (2) frequent hemoglobin and hematocrit evaluation, (3) replacement of estimated blood loss, (4) careful observation of vital signs, (5) nasogastric suction, and (6) antacid-feeding regimen.

The criteria for emergency surgery can be stated as follows although, of course, this must be individualized: (1) inability to stabilize vital signs with 1,500 cc. of whole blood, (2) recurrent hemorrhage, and (3) prolonged bleeding requiring daily transfusions of one liter or more.

Emergency surgery carries a much higher mortality rate than elective surgery. It is advantageous to carry the patient through the acute bleeding episode and if surgery is necessary, to do it electively. Certainly the surgeon would like to know the site of bleeding, which often remains a matter of conjecture during early management.

In the five-year period under study, our experience with massive bleeders consists of 79 patients admitted 83 times. Thirty-five of these patients underwent surgery, and 5 died. This represents 14% of those operated upon. Twenty-one, or 25% of the 79 patients died during their hospitalization. Of those dying, 16 of 21 were more than 70 years old. Our figure of 25% is almost identical with a recent report by Harkins and associates[4] in which 26% of 410 patients did not survive their period of hospitalization.

TABLE 2
SITE OF BLEEDING

Esophagus		14
esophagitis	1	
varices	10	
carcinoma	3	
Hiatus hernia		14
Stomach		46
gastritis	12	
benign ulcer	23	
benign neoplasm	1	
malignant neoplasm	10	
Duodenum		208
peptic ulcer	207	
malignant neoplasm	1	
Combined		18
esophageal varices and duodenal ulcer	2	
hiatus hernia plus ulcer	16	
Jejunum		16
stomal ulcer	2	
arteriovenous fistula, neoplasm or diverticulum	14	
Pancreas—malignant neoplasm		1
Biliary tract		1
Iatrogenic		18
anticoagulants	14	
steroids	3	
aspirin	1	
Stress		1
Unknown		28
TOTAL		365

The bleeding sites were as follows:

Dudodenal ulcer	5	Cancer—stomach	3
Gastric ulcer	4	duodenum	1
Varices	3	pancreas	1
Unknown	3	leukemia	1

After review of the medical records, we believed that 8 of these patients, mainly those with serious coexisting diseases and advanced age, would have been candidates for gastric cooling and could possibly have been salvaged.

Three patients who died from hemorrhage were in the hospital for an injury or other disease. This type of case is known to carry a high mortality. In 2 recently reported series, Ellison and associates[5] reported a 50% mortality and Dunphy and associates[6] a 63% mortality in this situation.

The surgical procedures done in the massive bleeder group are as follows:

Subtotal gastric resection	26
Vagotomy plus drainage procedure	4
Leiomyomectomy (stomach)	1
Gastrotomy and cholecystectomy	1
Laparotomy and biopsy	1
Resection of jejunum	2

A pertinent study was carried out by Dennis and associates[7] in which patients admitted to the hospital with massive gastroduodenal bleeding were placed randomly into 3 groups and treated accordingly. It should be noted that these were patients who were bleeding from the stomach or duodenum and included only peptic ulcer patients. The first group was one in which a nonoperative regimen was carried out. This program is based on the concept that hypovolemia and hypotension prevent the clot from being dislodged from the bleeding vessel. A quiet stomach persists in keeping the clot in place, and low gastric acidity prevents the clot from being digested. This is a method proposed by Andresen and was used before early surgery was proposed. In the second group, surgery was carried out as soon as feasible and almost without exception was done within twelve hours after admission. Only patients who are moribund from associated diseases were excluded from operation. The third group was called the selectively operative regimen, based on the concept that certain patients are more likely to die of hemorrhage than others. Patients more than 50 years of age or who have clinical evidence of arteriosclerosis are operated upon as soon as possible. If patients have had previous hemorrhage or do not respond to a predetermined amount of blood they too are operated upon at an early time. When these cases were analyzed it was found that the mortality rate in each group was essentially the same—14%. These figures were first published in 1958, and the study has been continued since that time. There still is no significant difference in the mortality between the groups.[8]

It is true that a conservative nonoperative regimen with careful observation is sufficient to handle patients who have not bled massively. The occasional patient who needs operation can be diagnosed accordingly. Elderly patients, especially those in the eighth and ninth decades of life, tolerate emergency surgery poorly, and it is necessary to be more conservative with these patients. Gastric hypothermia would seem to have its greatest usefulness in these patients.

Throughout the country there is a divergence of opinion as to the type of surgical procedure that should be done in these patients. Suture ligation of the bleeding vessel, along with vagotomy and pyloroplasty, has many advocates. In 1949, Joseph Weinberg[9] of the Long Beach Veterans Hospital inaugurated a program in which he proposed treating acute bleeders in this way. It was his feeling that direct surgical treatment was often avoided because of the high mortality and the need for a formidable procedure. In place of surgery, the physicians in attendance depended on rest, dietary restrictions, blood transfusions, and observation, hoping that the bleeding would cease. This method has substantially reduced the mortality rate in a series reported recently by Dunphy and associates.[6]

Wangensteen and associates[10] popularized the use of gastric hypothermia in the treatment of the peptic ulcer diathesis. Gastric cooling has been employed in the emergency treatment of massive upper gastrointestinal bleeding since 1958. Gastric freezing, on the other hand, is a newer procedure and is used for the elective and definitive treatment of some manifestations of peptic ulceration. Pyloric obstruction is essentially the only contraindication to this procedure. Local gastric cooling has been shown experimentally to reverse many of the factors responsible for hemorrhage in peptic ulceration. The procedure has been used also in esophageal varices, erosive gastritis, postoperative hemorrhage, which is usually a stress ulcer phenomenon, and in steroid ulcers. It has been attempted but works poorly in patients with blood dyscrasias and gastric tumors. Gastric cooling has controlled massive hemorrhage in approximately 80% of the cases due to duodenal ulcer and 60% of cases due to gastric ulcer. In 17 of 21 cases due to esophageal varices, the bleeding has been

controlled. Massive bleeding has been brought under control in 76% of their patients.

In recent months there has been a certain amount of disenchantment and criticism of gastric freezing. The criticism is directed to the use of gastric freezing for the treatment of the peptic ulcer diathesis because others have not been able to reproduce the results obtained by the Wangensteen group without serious complications. Dr. Wangensteen has repeatedly said that gastric freezing should only be done in large centers where there are teams of physicians capable of testing the procedure. Gastric cooling has a place in the control of massive bleeding but probably will not be used frequently in the community hospital until methods are simplified and standardized.

CONCLUSIONS

Severe bleeding which threatens the life of the patient is the most serious problem the surgeon and internist have to deal with in connection with peptic ulcer. Most cases of upper gastrointestinal bleeding are due to peptic ulcer, but at least 25% are not. Certainly, it is evident that the majority of the patients we see do not bleed massively and can be treated by a conservative, nonoperative program. In a few cases, a patient's life will depend on prompt surgical intervention. An accurate diagnosis is of extreme importance. We should be prepared to make use of endoscopic procedures if indicated and not restrict the use of emergency radiological studies. The surgeon must carefully search for and find the site and cause of bleeding to obviate an unnecessary "blind" gastrectomy. Lesions of the terminal esophagus and cardia, including those of the Mallory-Weiss syndrome, must be excluded. The incidence of lesions in the proximal small intestine indicates the need to carefully examine the small bowel before proceeding with definitive gastric operation. If gastric surgery is done, a properly timed and properly executed physiological operation must be chosen, and it seems that most surgeons will still prefer to do a standard gastric resection of Billroth type II or vagotomy plus hemigastrectomy. Vagotomy plus pyloroplasty and suture ligature of the bleeding site for duodenal ulcer is gaining in popularity. Without doubt, this subject will continue to be one of controversy and will be discussed and debated for years to come.

Massive upper gastrointestinal bleeding is a problem of major proportion. An overall mortality of 25% is significant and every effort must be made to lower it to the irreducible minimum.

SUMMARY

A statistical study of upper gastrointestinal hemorrhage over a five-year period is presented. Some of the problems in diagnosis and treatment are outlined with consideration of the practicability of gastric hypothermia in a community hospital.

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Assessment of Vasectomy as Means of Voluntary Sterilization

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THIS PAPER reviews 200 consecutive patients who had a vasectomy performed for the purpose of voluntary sterilization. A history of each couple included age, years married, number and age of children, miscarriages or abortions, religion, occupation, approximate income, and number of years of schooling. The reason for requesting the sterilization was also elicited.

A questionnaire was sent to each patient from one to four years later. The following questions were asked: (1) How long did you give vasectomy consideration before having the operation performed? (2) If you had it to do over, would you go through with it? (3) Since the operation, is the sex drive the same, greater, or less? (4) Is the family relationship the same, better, or worse? and (5) Would you recommend vasectomy as the best means of birth control? One hundred thirty-seven patients replied.

RESULTS

Information obtained from histories and questionnaires was tabulated. Table 1 shows the age distribution of the patients and their wives. The range was from 23 to 55, with a mean age of 34.7 years for the patients and 32.04 for the wives.

TABLE 1

AGE OF PATIENTS AND SPOUSES

Age	*Male*	*Female*
25 or less	5	15
26 to 30	53	51
31 to 35	50	61
36 to 40	49	48
40 or more	35	17

Table 2 shows the number of years married. More than 60% had been married more than ten years; the mean was twelve and one-half.

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TABLE 2

YEARS MARRIED

Five or less	18	11%
Five to ten	41	25%
Ten or more	108	64%
Total reporting	167	100%

Table 3 shows the number of children. The average was 4.1, with extremes of 1 to 12.

TABLE 3

NUMBER OF CHILDREN

Children	*Couples*
0	0
1	1
2	27
3	56
4	47
5	27
6	20
7	8
8 or more	5

Table 4 shows income spread. Average income was $8,154 per year.

TABLE 4

ANNUAL INCOME

Less than $5,000	17	12%
$5,000 to $10,000	100	70%
$10,000 and over	26	18%
Total reporting	143	100%

Table 5 shows educational spread. The total is greater than the number of patients because when information about the wife was supplied, it was included. The average number of years of schooling was thirteen and one-third.

TABLE 5

YEARS OF SCHOOLING

Less than twelve	54
Twelve (highschool graduate)	136
Thirteen to sixteen	91
More than sixteen	18
	299

Of the 200 patients, 140 gave socioeconomic reasons for requesting the vasectomy. The others cited medical reasons determined by their physicians, including Rh factor and mental illness or deficiency, in either mother or sibling. Approximately 60% were referred by the family physician.

In general, income of these patients was slightly above average. Average income for the Twin Cities metropolitan area was recently calculated at $6,840 and average years of education at ten and two-thirds. Average income of the 200 patients was $8,154 and years of education thirteen and one-fourth. The average number of living children—4.01—was considerably higher than the national average—2.8. This series would appear to represent a cross section of the population from which it was derived and, as a group, to have more than fulfilled its responsibility to propagation of the race.

FOLLOW-UP QUESTIONNAIRE

One hundred thirty-seven patients replied to the follow-up questionnaire. To the question, "How long did you give vasectomy consideration before having the operation performed?" the average patient and spouse reported less than two years. Many commented that they would have acted earlier if they could have found a willing practitioner. To the question, "If you had it to do over, would you go through with it?" 134 replied in the affirmative and 3 in the negative. One who stated he would not go through with it again had confused the procedure with castration. A hematoma developed in another who apparently suffered considerable discomfort. A third who replied negatively gave no reason. The commonest complaint (5.5%) was skin diastasis with minimal to moderate infection. Four patients required antibiotics, and 2 were hospitalized because of complications. It must be kept in mind that these figures may be incomplete, inasmuch as some 15% of patients were followed by their own physicians and the exact postoperative course was not known.

Replies to the question, "Since the operation, is the sex drive the same, greater, or less?" are shown in table 6. About 97% felt that libido was as great or greater.

TABLE 6

POSTOPERATIVE SEX DRIVE

Same	101	73%
Greater	31	24%
Less	5	3%

Regarding family relationship, 74% felt it was better, 24% unchanged, and 2% worse.

A last question, "Would you recommend vasectomy as the best means of birth control?" was answered affirmatively by 92%. In many cases the answer was qualified, indicating this procedure would be best if and when, in the patient's mind, the desired family size had been obtained.

DISCUSSION

Voluntary sterilization by vasectomy would appear to be a most effective method of birth control. No attempt is made to compare it with others. Although not as trivial as many times stated, the operation is minor when compared with the major surgery necessary in women. The sample examined would appear to be a representative cross section of the Upper Midwest urban population. There seemed to be little or no desire on the part of couples without children to have the procedure carried out. The average number of children per family was well above the average for the nation.

SUMMARY

Vasectomy was performed in 200 patients, largely to limit family size. The vast majority were satisfied and stated they would recommend it to others.

The Psychiatry of Presidential Assassination

Part II: Garfield and McKinley

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PRESIDENT JAMES A. GARFIELD AND CHARLES J. GUITEAU, JULY 2, 1881

Charles J. Guiteau was a small, quick, nervous man who had a remarkably checkered career: lawyer, evangelist, insurance salesman, author, publisher, and swindler. Born in Freeport, Ill., on September 8, 1841, he was 40 years old when he pulled the trigger of a .44-caliber British bulldog revolver and mortally wounded President James A. Garfield.

Charles' mother died when he was 7. His father, Luther W. Guiteau, of Huguenot descent, was public-spirited and much interested in religion and Republicanism. He held several elected offices in Freeport, including that of county superintendent of schools. He was an ardent member of the Oneida Community, whose leader, the Reverend John H. Noyes, believed that the Second Coming had already occurred over Jerusalem at the time of its destruction by the Romans in A.D. 70 and hence that man could achieve a union with Christ now. Luther Guiteau had a long-standing conviction, which properly must be regarded as a delusion and therefore as a symptom of mental illness, that he was immortal. The Guiteau family had more than its share of mental illness: a brother of Luther was psychotic and two sisters were possibly so. A niece and a nephew, first cousins of the assassin, were committed to mental hospitals.

Young Charles adopted his father's belief in divine inspiration. This childhood concept was to become an overt and tragic symptom of his mental illness: God, he would later say, had commanded him to kill the President. His father, however, lived a useful life, dying at age 70 a well-esteemed person in Freeport. A letter written by the elder Guiteau to his other son, John W., on March 30, 1873 (eight years before the assassination), is of great interest, especially considering the amount of mental illness Luther had seen in his own family. Referring to Charles, the anguished father wrote:

> I have been ready to believe him capable of almost any folly, stupidity or rascality. The one possible excuse that I can render for him is that he is insane. Indeed, if I were called as witness upon the stand, I am inclined to think I should testify that he is absolutely insane and is hardly responsible for his acts. My own impression is that unless something shall stop him in his folly and mad career he will become hopelessly insane and a fit subject for the lunatic asylum. Before I finally gave him up I had exhausted all my powers of reason and persuasion, as well as other resources, in endeavoring to control his actions and thoughts, but without avail. I found he was deceitful and could not be depended upon in anything, stubborn, wilful, conceited and at all times outrageously wicked, apparently possessed of the devil. I saw him once or twice when it seemed to me he was willing to do almost anything wicked he should happen to take fancy to. You will remember . . . I told you to keep clear of him and not have anything to do with him. Should anybody ask about him now, I should be compelled to say to them that I thought he was insane, or at least a monomaniac, and should there leave it and say no more about him. His insanity is of such a character that he is as likely to become a sly, cunning desperado as anything. . . . So I, you see, regard his case as hopeless, or nearly so, and of course know no other way but to dismiss him entirely from my mind and leave him entirely in the hands of his Maker, with a very faint hope that he can be changed either in this world or the next.[5]

As his father's letter points out, Charles Guiteau had a long record of psychopathic behavior. He daydreamed excessively, accomplished little, and disregarded his young wife. He was admitted to the bar in Chicago in 1868 after passing a skimpy oral examination. In a larceny case in Chicago to which he had been assigned, his brother-in-law later reported, Guiteau made such a rambling speech that he convinced the district attorney he was insane. Although his emotional instability went back to his early years, overt symptoms of illness apparently began to develop about 1872, at age 31. After some minor work in politics that year, he decided that

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he would be the proper person to become a diplomatic representative.

In 1874, after not quite five years of marriage, Guiteau's wife divorced him, and whatever small stabilizing influence she had was now gone. His church expelled him upon learning that he had known several women sexually during his marriage and that he had contracted syphilis. (No evidence exists that he had syphilitic brain disease.) As if these blows were not enough, a New York newspaper exposed his fraudulent methods of collecting legal fees, nearly putting an end to his career.

From this point on, Guiteau's course was continuously downhill, signs and symptoms of schizophrenic regression becoming apparent. In December of 1874 he was arrested and imprisoned for five weeks for defrauding a hotel, one of many he had left without paying his bill. On his release, he went to Chicago, identifying himself as a lawyer who had recently resigned as United States Consul in Marseilles. His French name lent backing to this lie.

In 1877 Guiteau began traveling around the East and Middle West, giving lectures on religion to small audiences and trying to sell his remarks in pamphlet form. (At his trial his attorney produced some people who had gone to listen, and all agreed that the content and method of delivery suggested insanity in the speaker.) He ran out on many hotel and printers' bills. He routinely rode trains without a ticket; when the conductor asked for one, he would reply that he was on the business of the Lord. He was usually allowed to ride as far as the next station, but on two occasions he had to jump off moving trains to escape arrest. Because he felt the world owed him a living (a feeling probably based on a delusion of grandeur—that of being God's agent), he victimized everyone he could. During this period he began to think that he would be President of the United States some day.

By late spring of 1880, his lecture audiences having dwindled and a return to insurance selling having proved unfruitful, Guiteau was desperately searching for a way out of his failures. The excitement building up over the coming Republican National Convention in Chicago overtook him, apparently reminding him of his past political fantasies and dreams of power. He departed for New York City on June 11, 1880, thinking to offer his services to the Republicans. He did so, he said later, with "the distinct feeling that I was on my way to the White House. . . ."

He hung around several campaign headquarters, passing out copies of a rambling speech he had written that he fancied was to plot the policy for the Republican party. (After the election, Guiteau said his speech had put Garfield into office.) He did not realize that he was regarded as a nuisance and a crackpot. In October 1880, a month before the election, he wrote to Garfield that he would be willing to accept the ambassadorship to Austria and that he was going to marry a wealthy woman.

On the day after the inauguration Guiteau borrowed $10 from an insurance clerk and went to Washington to obtain, as he felt sure he would, the Paris consulship. He stayed at some of the best Washington boardinghouses, giving the names of the President and the Secretary of State as references and leaving without paying his bills. Nearly every morning he would go to the White House, take a sheet of stationery, write his request for the consulship, and give the note to one of the secretaries to present to the President. Next he would leave a similar note at the Secretary of State's office. The rest of the day he spent asking members of Congress to sign a petition recommending him for the Paris consulship. None did. By mid-May, after a long period of either patience or poor management, the White House staff had been instructed to keep him out.

In sharp contrast with his fantasy life as a prospective foreign representative, Guiteau's actual life was one of deterioration and abject failure. Unkempt in appearance, he sometimes wore no socks and often kept his coat collar turned up to hide the fact that he had no shirt collar. Sometimes he changed what clothes he had behind bushes in Washington parks.

In an interview after the assassination, Guiteau told how the idea of "removing" the President came to him: "On . . . Wednesday [May 18, 1881] . . . I felt depressed and perplexed on account of the political situation, and I retired much earlier than usual. I felt wearied in mind and body, . . . and I was thinking over the political situation, and the idea flashed through my brain that if the President was out of the way everything would go better. At first this was a mere impression. It startled me, but the next morning it came to me with renewed force. . . ."[5] On May 23 he sent a letter to the President condemning James G. Blaine, the Secretary of State, and demanding his immediate resignation. If made today, one statement in this letter would receive the attention of the Secret Service: ". . . otherwise you and the Republican Party will come to grief." Talking of this period at his trial, Guiteau said that God had directed him

to kill the President, leaving the details of the assassination to him.

On June 8 he purchased a self-cocking, .44-caliber, 5-shot British bulldog revolver and a box of cartridges. The owner of the gunshop showed him how to load the revolver (Guiteau, unlike Lawrence, knew nothing of firearms), suggested he practice in a wooded area along the Potomac a few blocks from the White House, and assured him that the gun was large enough to "kill a horse." On two occasions Guiteau practiced firing at saplings.

Guiteau frequently followed or waited for the President and, he said, had several good occasions to shoot him. At least twice, sultry weather kept him from carrying out the act. Once he did not shoot because Mrs. Garfield, accompanying the President, looked frail and worn. On another occasion, when Garfield was in church, he was afraid a shot would injure someone else. He liked the idea of shooting the President in church, however, because the setting seemed to be ideal for executing the will of God.

Learning from the newspapers that the President was leaving by train at 9:30 A.M. on July 2 for a two-week vacation, Guiteau waited for him in the station. (A few days earlier he had called at the District of Columbia jail to see what kind of accommodations he would have. Fearing that he would be mobbed after the shooting, he had, on arriving at the station, hired a hack driver to wait outside to take him within running distance of the jail.) Guiteau let the President pass by, then walked up behind him and fired at his back. "My God! what is this?" Garfield exclaimed. As the President started to fall, Guiteau fired again; the bullet narrowly missed. Guiteau was quickly caught by a policeman and escorted from the building. The first bullet had fractured two of the President's ribs and the first lumbar vertebra and had cut a large artery. Garfield lingered until 10:35 P.M., September 19, 1881.

Guiteau gave this explanation of his motives:

> I think of General Garfield's condition as a removal and not as an assassination. My idea simply stated was to remove as easily as possible Mr. James A. Garfield, a quiet and good-natured citizen of Ohio, who temporarily occupied the position of President of the United States, and substitute in his place Mr. Chester A. Arthur, of New York, a distinguished and highly estimable gentleman.
>
> Mr. Garfield I intended to quietly remove to Paradise (which is a great improvement on this world), while Mr. Arthur saved the Republic. . . . Not a soul in the universe knew of my purpose to remove the President. If it has failed I shall never attempt it again. My motive was purely political and patriotic, and I acted under divine pressure. It was the same kind of pressure that led Abraham to sacrifice his son Isaac. . . . The President's nomination was an act of God; his election was an act of God; his removal is an act of God. These three specific acts of the Deity may give the clergy a text.[5]

During his trial Guiteau interrupted witnesses, made rude remarks, dressed down his attorneys, and defied Judge Walter S. Cox's orders to remain quiet. At one point the exasperated judge threatened to have his mouth gagged to keep him quiet, but his words had no effect. Judge Cox was harshly criticized for permitting the prisoner to misbehave. At the opening of the trial on November 14, Guiteau announced to Judge Cox, "I come here in the capacity of an agent of the Diety in this matter." On another occasion he informed the court, "I expect an act of God that will blow this court and jury out of that window if it is necessary." Some persons thought Guiteau's behavior was an attempt to feign insanity.

The lawyers for the defense tried hard to prove that Guiteau really was insane. Their key medical witness, Dr. Edward C. Spitzka, a young neurologist, later wrote:

> To the reflecting psychologist, . . . the readiness with which Guiteau accepted bogus checks for fabulous sums, in sober earnest, while in prison, his childish indignation at the written curses, threats, miniature gallows and hempen rope sent him by mail; his belief that the persons visiting him from motives of curiosity were his admirers; his replies to alleged candidates for his hand in marriage, and so on, are among the strong cumulative evidences of his insanity. . . .
>
> . . . . . .
>
> . . . Guiteau . . . was not a responsible agent when he killed President Garfield. . . . Because Guiteau was insane, he believed that his foul deed was a meritorious act; because he was insane, he believed that he could commit that crime and not only escape punishment, but earn the gratitude of a nation; and because he was insane, when he had no refuge on earth left, he turned to a future which, if he had been sane, would have held out little of the consolatory to him, and arrogated to himself in the other world a position side by side with the Almighty—and in this a monument erected by a grateful and contrite nation, after the long and bloody war he predicted would grow out of his execution. Could sane conceit and sane egotism ever approach this? Could the check of the law ever be applied so as to influence such overwhelming self-exaltation?[6]

Another witness for the defense, Guiteau's sister, said that he had once threatened her with an ax and that afterward the family physician had declared her brother to be insane, but harmlessly so. Even though his life depended on it, however, Guiteau denied in court that he was a lunatic. Instead, he claimed to be a patriot acting under the specific direction of the Lord. "Nothing that the Diety directs a man to do can violate any law," he exclaimed in a speech to the jury.

Reminiscent of the killing of Oswald by Jack Ruby, two attempts were made on Guiteau's life

after the assassination. The first attempt was on September 11 while Guiteau was in his jail cell at the Old Capitol prison on the bank of the Anacostia River. Several of the soldiers assigned to guard the jail decided that the prisoner should die, and the duty of firing the shot fell to Sergeant John A. Mason, Company B, Second Artillery. He fired at Guiteau's head when it appeared in the cell window. Missing Guiteau, the bullet shattered a picture of his mother that he had in his cell. The second attempt to shoot him was made when he was being transported in a prison van during the course of the trial. A mounted rider fired a revolver bullet into the van but miscalculated Guiteau's position. The bullet bruised the prisoner's left arm.

The two attempts to kill Guiteau met with widespread approval; he was thoroughly detested by the public. Occasionally, however, a sober voice was raised, a voice that was to be heard again eighty-two years later when Jack Ruby killed President Kennedy's assassin. A prominent Washington businessman said about the second attempt on Guiteau's life:

> I am sorry it should have taken place, for it can only add to the wretchedness of the whole thing. We are disgraced as a nation by such an occurrence.
>
> What will foreigners think of us? The assassination of the 2d of July was a dreadful calamity, but then we can look upon that as the freak of a lunatic or the desperate act of a dangerous and baffled man. But now, when that man is on trial for his life and the judicial hearing is proceeding in a regular way, and with no danger of any but a perfectly just and fair conclusion, to have someone take upon himself the office of executioner is entirely inexcusable. It begins to look as if we were in fact a lawless community. . . . This Washington fool steps up and insults every law-abiding citizen of the land by his act.[6]

Another man with a sober voice, a prominent member of the New York bar, would have been interested to reread on November 25, 1963, could he have done so, what he said in 1881: "It is surprising that any one should forget that Washington is not in the backwoods of Texas, and that Judge Lynch is not a member of the Washington judiciary. Suppose that Guiteau had been removed by this new assassin's bullet, what then? Why, American citizens of every class would be placed under the disgrace of not being able to conduct a simple trial. . . . To shoot at him now merely shows that there is some other simpleton as crazy for notoriety as Guiteau himself."[5]

The jury took a little longer than an hour to find Guiteau sane and guilty. A group of citizens interested in the humane treatment of the insane applied to Associate Justice Joseph P. Bradley of the Supreme Court for a writ of habeas corpus. It was denied, and President Chester A. Arthur refused to grant a reprieve. Shortly after noon on June 30, 1882, Guiteau stood on the scaffold, reciting a poem he had written that morning. When the trap opened, he was chanting, "Glory, glory, glory. . . ."

The life history of Guiteau leads me to the opinion that the psychiatric diagnosis is schizophrenic reaction and that, like Richard Lawrence, Guiteau should have been committed to a mental hospital rather than executed. The jury, however, were reflecting the public's hatred of Guiteau and his act.

PRESIDENT WILLIAM McKINLEY AND LEON F. CZOLGOSZ, SEPTEMBER 6, 1901

Twenty years after the Garfield murder and the ten-week trial of Guiteau, in which the verdict of guilty was reached after only sixty-five minutes of deliberation, Leon F. Czolgosz shot and killed President William McKinley. The execution of justice was even faster in the case of this assassin. The entire trial, including impaneling the jury, took not quite eight and one-half hours. The jury deliberated only thirty-four minutes before finding the prisoner guilty. There was no defense of insanity, because his reluctant attorneys never raised the question. That he was psychotic is certain, but so eager was the public for his scalp that no matter what had happened at the trial, the outcome would have been the same. The trial is a conspicuous blot on the record of American justice. Czolgosz was condemned before it started.

Czolgosz shot President McKinley without much trouble and with a small amount of preparation. Already determined on his course of action, he read that McKinley would attend the Pan-American Exposition in Buffalo and that on the afternoon of September 6, 1901, he would hold a public reception at the Temple of Music. A trusting soul who could not believe that anyone would want to hurt him, McKinley had overruled his staff's attempts to cancel the reception. Czolgosz joined the line on that warm afternoon, a loaded .32-caliber Iver Johnson revolver in his hip pocket. Approaching McKinley, he deftly drew the gun and wrapped it into his right hand with a handkerchief, giving the appearance of a bandaged hand. At 4:07 P.M., as the President held out his hand to him, Czolgosz fired twice through the handkerchief. One bullet hit McKinley in the sternum; the other perforated the abdomen and both walls of the stomach, lodging behind the pancreas. The President shivered, stood to his full height, looked at his murderer with astonishment, and slumped into the

arms of the men around him. The range was so close that McKinley's vest was powder-burned. Mobbed and beaten, Czolgosz muttered, "I done my duty." When McKinley died eight days later, Theodore Roosevelt became President. He would meet, eleven years later in Milwaukee, John N. Schrank, who would hit but not kill him with a .38-caliber bullet. After the death of McKinley, no attempt at assassination was to be successful until November 22, 1963.

In 1901 anarchists were to be found everywhere. At first Czolgosz was identified as one of them and his deed as an anarchist plot; his own admission that he was an anarchist was not questioned. It is true that he had approached several anarchist leaders and was attracted by their teachings. But the anarchists were disconcerted by his strange behavior, ignorance of their doctrine, and use of an alias. Several days before the assassination, one of their newspapers printed a description of Czolgosz with a warning that he was a spy.

In the Buffalo police station after the shooting, Czolgosz said he carried no grudge against the President but that he did not believe in republican government, rulers, voting, religion, or marriage. In a confession that night he wrote, "I killed President McKinley because I done my duty. I don't believe one man should have so much service and another man should have none." Later he called the President "an enemy of the good working people" and said, "I thought it would be a good thing for the country to kill the President." Within forty-five days after the President's death, Czolgosz was tried, found guilty, and electrocuted. As a final disgrace, a carboy of sulfuric acid was poured into his coffin after it had been put into the grave.

The trial is of brief interest. Five physicians, three for the prosecution and two for the defense, testified that Czolgosz was sane and responsible for his act. Czolgosz had two court-appointed attorneys, retired justices of the state supreme court. They took his case with a great show of reluctance, expressing sympathy for the slain President. Other than the two physicians who said the defendant was sane, the defense had no witnesses; Czolgosz refused to testify. He received the guilty verdict without emotion. No appeal was filed. Prosecution and defense alike congratulated themselves on the speedy fairness of American justice; most of the press joined in.

Dr. Allen McLane Hamilton summed up Czolgosz's trial:

> The limit of tolerance was reached in the Guiteau case, but Czolgosz was hurried to death. The jury were in the room and heard the almost pharisaical protests of the two elderly judges assigned to the defense. It was just as much their duty to vigorously defend Czolgosz as it is a doctor's duty to succor a dying thief or a priest's to shrive a dying magdalen. Neither public opinion nor the personality of the victim should have influenced the lawyers. . . .
>
> The assassin was really a defective who had long been drifting to paranoia, and whose actual delusions of persecution and grandeur found soil in which to grow. As early as the spring of 1901 his family said he had "gone to pieces"; he neglected his trade and became a vagabond; he had delusions that he was being poisoned, for he bought and cooked his own food, and would not let even his mother prepare his meals. He talked a great deal about anarchy and murder, and eagerly read the accounts of the assassination of King Humbert; he likewise had religious and "exalted" delusions. . . .
>
> In the electric chair his last words, I learn, were an expression of his delusions, which he consistently held to the last, and he died believing himself to be a martyr.[7]

The medical experts who testified at the trial apparently accepted without investigation Czolgosz's own statements that he was an anarchist and was not insane. One of them, Dr. Carlos F. MacDonald, writing about the kangaroo-court setting, said, "Had Czolgosz been on trial for the murder of a common citizen, instead of the President, it is safe to say that not one of the jury as completed would have been accepted by the defense. . . ."[9] Nevertheless, not bothering to look into Czolgosz's mental background, Dr. MacDonald testified that the assassin was not insane. He stated that pre-trial examinations revealed no evidence of mental disease, that, in fact, the results indicated Czolgosz was a victim of anarchy, a "social disease"!

About a year after Czolgosz was electrocuted, two psychiatrists, realizing that his life had not been studied, undertook at their own expense to obtain medical and psychiatric data on him. Dr. Walter Channing, a professor at Tufts Medical School in Boston, was the senior member. Dr. L. Vernon Briggs did most of the field work, interviewing friends, relatives, employers, and anyone else he could find who had known the assassin. Their publications[7,8] are the only thorough personality studies of Czolgosz. After analyzing their collected data, Drs. Channing and Briggs concluded that Czolgosz was insane at the time he pulled the trigger.

Leon Czolgosz was born in Detroit in 1873, four months after his parents had arrived from Poland. His father had obtained a job in the city sewer system, and his mother took in washing. Leon was the fourth child. After the eighth baby was born, when Leon was 12, his mother died. A quiet boy who stayed largely to himself, Leon became more shy as he grew older. He had no close friend except Waldek, his older brother.

From 1891 through 1898 Leon was employed

by a Cleveland wire mill. According to his foreman, he was a steady worker who kept out of mischief. In 1893 the workers in the mill struck for more pay. Returning to the mill after the strike, Czolgosz assumed the name of Fred C. Nieman, because he was afraid a new supervisor had learned that he was a troublemaker. (Nieman was to be the first name he gave the police upon his apprehension after the shooting.) During the strike he and his brother Waldek, reared as Catholics, prayed hard that it would be settled. Feeling that their efforts brought no results, they began to have serious doubts about their religion. Leon became suspicious of priests, believing that they were deliberately deceiving him.

Persons knowing Czolgosz in 1895 thought he was remote, sluggish, and lacking in zest and fun. In retrospect, this period, when he was 22 years old, undoubtedly marks the onset of his mental illness. He was fastidious; he would not step on a worm or kill flies. Until 1898, however, he was never regarded as being ill. Then, at age 25, he suffered a "nervous breakdown" that changed him from a reasonably normal and industrious young man into a sickly and abnormal one. He quit his job, and one of his brothers noted that he was "so gone to pieces like and . . . so pale." He never again had a steady job, never really tried to find one. Becoming more bashful and preoccupied, he retired to the family farm and spent the days brooding and reading newspapers. He slept a great deal, often under a tree or on the porch, waking up briefly and drifting off to sleep again. Every so often he went to Cleveland to see a doctor, but he refused to be put into a hospital. "There is no place in the hospital for poor people," he told his brother Waldek. "If you have lots of money, you will get well taken care of." At about this stage, probably because he was under the delusion that his food was being poisoned or at least tampered with, he began preparing his own food and eating apart from the family. The assassination of King Humbert I of Italy on July 29, 1900, by an anarchist from Paterson, N.J., fascinated Czolgosz; he read and reread a newspaper account of the event, taking it to bed with him.

Czolgosz spent July and August of 1901 in a boarding house in West Seneca, a small town near Buffalo. A few days before the President was to appear at the Pan-American Exposition, Czolgosz checked out of the rooming house, paying part of his bill with a broken revolver. He rented a cheap room in Buffalo over a saloon and bought another revolver for $4.50. This was the Iver Johnson that a few days later was to give him a place in history as the assassin of an American President.

Several other observations on Czolgosz are of psychiatric interest:

- For several months before the murder he would not answer people for a long time; he was apparently deep in thought.
- He went to extremes in cleanliness. Asked, after arrest, to show how he had concealed the revolver, he refused to do so until given a fresh handkerchief. Milk and water that he drank had to be absolutely clear.
- He much preferred being by himself and avoided the company of others. He never had a girl friend insofar as is known.
- Just before his electrocution he said that he killed the President for the good of the working people and that he had no regrets. He was only sorry that he could not see his father before he died.

The various data about Czolgosz add up, in my opinion, to a diagnosis of schizophrenia. I feel that he was psychotic, insane in the eyes of the law, and that the appropriate action would have been commitment to a mental hospital.

(To be continued in May)

Extramedullary Plasmocytoma of the Lung

Report of a Case

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EXTRAMEDULLARY PLASMOCYTOMA (extramedullary myeloma, plasma cell tumor, plasmocytoma, or plasmoma) is a rare tumor occurring primarily in any part or organ of the body outside the bone marrow. It is mostly found in the region where the lymphoid tissues are abundant, for example, in the floor of the mouth, soft palate, tonsils, or upper respiratory tract, and has been reported by many authors.[1–8] Other sites include the skin, conjunctiva, lymph node, thyroid gland, stomach, intestine, ovary, and spermatic cord, but primary localization in the lung is very rarely encountered.

CASE REPORT

A 24-year-old Thai male was admitted to the surgical department of Siriraj Hospital, Bangkok, on Feb. 3, 1962, with a round shadow in the lower lobe of the right lung on routine X-ray examination. He did not have any past history of lung diseases and was free from fever, chest pain, dyspnea, and chronic cough. There was a slight weight loss during the last two months without disturbance of gastrointestinal or urinary function. Family history was not contributory. He had just graduated from the Bangkok Technical School in the field of engineering and was preparing to go abroad when the chest film discovered the lesion.

Physical examination on admission. The temperature was 36.2° C.; pulse, 78; respiration, 20; and blood pressure, 140/90 (right arm). He was well developed, well nourished, and healthy, with neither jaundice nor cyanosis. Superficial lymph nodes were not enlarged. The respiratory and other systems were not remarkable.

Blood examination. Hemoglobin was 14.4 gm. percent; red blood cell count was 4,780,000 per cubic millimeter. White cell count was 11,900 per cubic millimeter, with 64% neutrophils, 33% lymphocytes, 2% monocytes, and 1% eosinophils. Blood platelets were adequate.

Blood chemistry. Serum albumin was 4.3 gm. percent and globulin, 2.8 gm. percent. Nonprotein nitrogen was 26.5 mg. percent. Creatinine was 1.2 mg. percent. Sugar was 80 mg. percent.

Urine examination was negative; Bence-Jones protein was not detected. Examination of feces was also negative.

X-ray examination of the chest revealed a large, round shadow (coin lesion) about 5 cm. in diameter in the lower lobe of the right lung (Fig. 1).

Operation. Two days after admission, exploratory thoracotomy was performed via the right sixth intercostal space through the pleural cavity. There was no pleural adhesion. Palpation revealed a firm, spherical mass about 5 cm. in diameter occupying the periphery of the middle and posterior basal segments of the right lower lobe. The pulmonary fissures were clear. The hilar lymph nodes were not enlarged. The entire lower lobe was resected. The operative and postoperative courses were uneventful, and the patient was discharged on the eleventh postoperative day.

Pathological report: Macroscopic findings. The specimen received was the entire lobe of the lung, measuring $13 \times 11 \times 3.5$ cm. The pleural surfaces were smooth and glistening except for a small, depressed scar on the posterobasal aspect. On cutting through it, a rounded, grayish-white tumor with rubbery-firm consistency was found, measuring 4.8×4.5 cm. The mass was not distinctly encapsulated but well circumscribed. It was separated from the surrounding lung tissue by a thin layer of white tissue. The cut surface was finely granular and showed no

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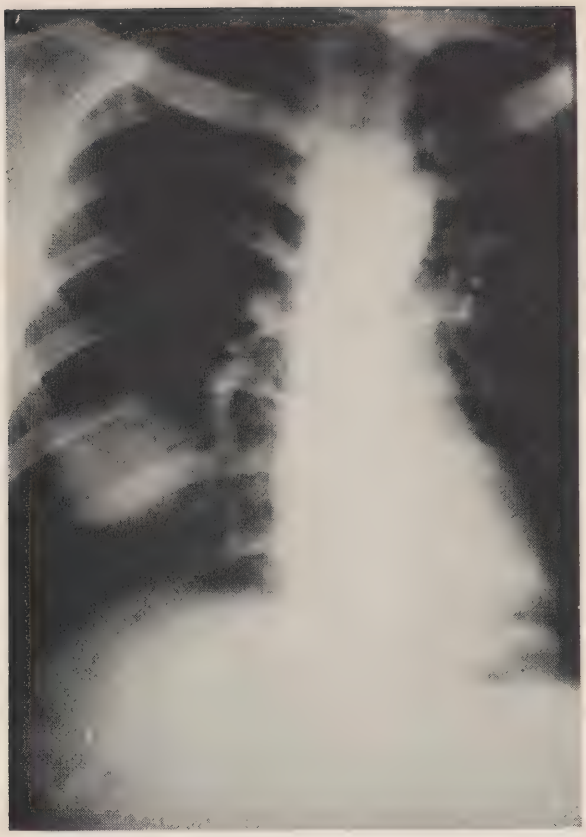


Fig. 1. X-ray film of chest showing large, round shadow in lower lobe of right lung

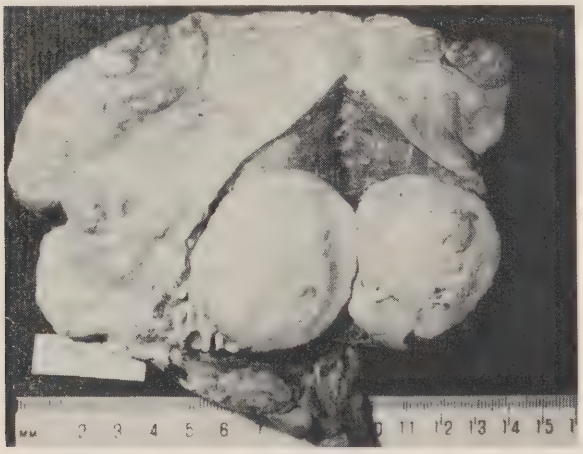


Fig. 2. Surgical specimen of entire lower lobe of right lung showing firm spherical mass occupying middle and posterior basal segments

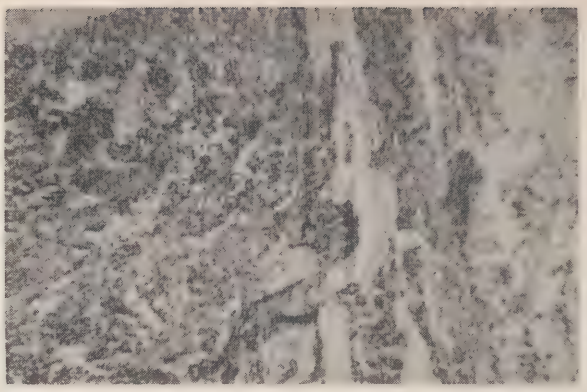


Fig. 3. Microscopic appearance showing cellular tumor (left) compressing normal lung tissue (right). Hematoxylin and eosin, × 35

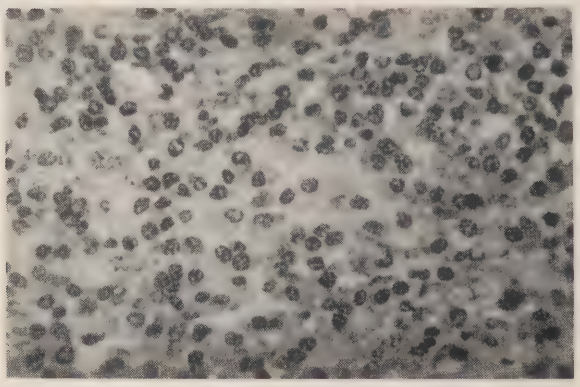


Fig. 4. Tumor consisting mainly of mature plasma cells. Hematoxylin and eosin, × 450

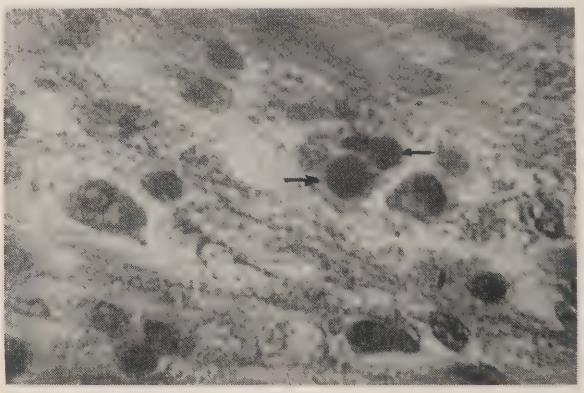


Fig. 5. (Arrows) Large acidophilic, hyaline, rounded masses, so-called Russell bodies, outside tumor cells. Hematoxylin and eosin, × 1,000

necrosis or hemorrhage. The segmental bronchi and lung tissue around the lesion were compressed (Fig. 2).

Microscopic findings. The tumor was highly cellular. It consisted mostly of small oval or round cells, with thin, delicate stroma of collagen fibers and few vascular channels. The cells mentioned were identified as mature plasma cells, with a few immature forms, by the characteristic large, round nucleus and peripheral distribution of the chromatin, showing the "cartwheel" pattern. The cytoplasm was amphoteric. A few large acidophilic hyaline rounded masses, the so-called Russell bodies, were found both inside and outside the tumor cells. By the Masson trichrome technique these bodies were deep red. There

were some collections of lymphocytes among the plasma cells. The tumor had no true capsule but was separated from the neighboring lung tissue by a few delicate collagen fibers and at other places by a few distorted bronchioles. Atelectasis was noted (Figs. 3, 4, and 5).

DISCUSSION

The real nature of plasmocytoma is not certain. Many authors express different opinions. The condition is considered a granuloma secondary to chronic inflammation, benign tumor, or malignant tumor due to variations in behavior of the tumor. It may turn out in the late stage to be multiple myeloma. Romanoff[9] found that most of the extramedullary plasmocytoma was highly malignant but behaved initially as a benign tumor. Hellwig[10] and Hill and White[11] suggested that it was impossible to decide whether the tumor was benign or malignant in any case without evidence of recurrence or metastasis.

Extramedullary plasmocytoma of the lung was first reported by Gordon and Walker[12] in 1944. At present there are only 16 reported cases.[9,13] Follow-up studies were made on the patients whose lungs were unilaterally pneumonectomized or lobectomized and, on another patient, where the tumor was only enucleated. The results showed that 1 patient still survived eight years postoperatively, 1 died within one year because of empyema and bronchopneumonia but not from the tumor, 1 with enucleation presented a local recurrence of the tumor within eight months, and 1 showed multiple metastases and died twenty-two months later. The rest in the record survived with varying durations. This patient has been well and healthy eighteen months postoperatively.

SUMMARY

The authors report a 24-year-old Thai male with primary extramedullary plasmocytoma of the lung that was unexpectedly found on routine X-ray examination of the chest. Right lower lobectomy was performed, and the patient is still well eighteen months after operation. This location of the tumor is very rare, and only 16 cases have been reported. The exact nature of the tumor is unknown.

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WHEAT GLUTEN ANTIBODIES are found in circulation of patients with nontropical sprue. Malfunction in intestinal mucosa cells results in incompletely degraded polypeptides which enter circulation and stimulate antibody production. Fifteen of 17 nontropical sprue patients on a gluten diet had antibodies to gluten fraction III, which disappeared in all but 1 after change to a gluten-free diet. None of 90 controls with other diseases had antibodies to fraction III.

DONATO ALARCÓN-SEGOVIA, M.D., TEODORO HERSKOVIC, M.D., KHALIL G. WAKIM, M.D., PAUL A. GREEN, M.D., and HAROLD H. SCUDAMORE, M.D., Mayo Clinic and Foundation, Rochester, Minn.
Amer. J. Med. 36:485-499, 1964.

Section on PAIN and DISTRESS

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Interdisciplinary cooperation

As physicians we should be as well informed as possible about the advantages to be obtained in cooperating with the dental profession.

In order to obtain optimal results for patients who must be treated by both physician and dentist, it is well for us to keep in touch with what they are doing.

In this issue an effort is being made to follow up this idea.

JOHN S. LUNDY, M.D.

General Anesthesia and Analgesia

Application and Use in Present-Day Oral Surgery

THOMAS M. TERPINAS, D.D.S., and JOHN S. LUNDY, M.D.
San Mateo, California, and Seattle

CURRENT SURGICAL TECHNIQUES would not be possible without the present-day development of the art and science of anesthesiology. In few other fields of medicine is it possible to maintain and preserve the patient's life and general welfare so carefully and successfully as in anesthesia and analgesia. In dentistry it has become readily apparent that the application of general anesthesia to oral surgery is of prime importance.

TRAINING OF DENTISTS IN GENERAL ANESTHESIA

Throughout the country at various postgraduate centers dentists are taught the basic principles of general anesthesia. These practitioners have undertaken to study anesthesiology in relation to oral surgery and to apply it clinically with the cooperation of the physician-anesthesiologist. Under these conditions the dentist learns to evaluate the condition of his patient during surgical procedures and to learn how the anesthesia can be accommodated to the type of operation which is to be performed. He learns how to treat patients during periods of difficulty and how to recognize the various untoward reactions which may occur during anesthesia.

The fact that institutions have been developed for the teaching of dentists in basic clinical anesthesia attests to the great need in dentistry for well-trained dental anesthesiologists. This part of the training should be and is carried out with

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the direct cooperation and guidance of the medical anesthesiologist.

ECONOMIC FACTORS OF ANESTHESIA IN DENTAL PRACTICE

On the other hand, to require a physician to produce general anesthesia in the oral surgical office is a functional and financial encumbrance upon the patient as well as the physician. This readily becomes apparent when it is considered that from the standpoint of numbers of patients alone, there are too few physician-anesthesiologists to meet the demands of heavy operating schedules in hospitals, as well as in busy oral surgical practices in which as many as 6 to 15 sessions of general anesthesia may be required in a single day. The crowded conditions of our hospitals are only too well known to us all, so that it is not difficult to imagine the many problems which would inevitably arise from any increases in the surgical load. From the standpoint of efficiency, speed, and organization, as many as possible of these procedures must be carried out in the dental office. Furthermore, the challenging economics of the situation become self-evident when the overall cost of an oral surgical procedure performed in the hospital is compared with the cost of one performed in the office on an outpatient basis.

EVOLUTION OF ANESTHESIA FOR ORAL SURGERY

The evolutionary and technical development of anesthesia for oral surgical procedures roughly has paralleled the methods developed for other surgical specialties. It has now been a little more than a century since Dr. Horace G. Wells, a Hartford dentist, introduced nitrous oxide as an agent for the production of surgical anesthesia.[1] Since that time the controversy over the anesthetic qualities of this agent has continued without respite. Condemnation or acceptance of nitrous oxide has been in large part governed by the individual clinical skill of the anesthesiologist.

The first recorded use of oxygen combined with nitrous oxide took place in 1868 in the hands of Andrews,[2] a Chicago surgeon. In 1878 Paul Bert[3] in France reported the administration of a mixture of nitrous oxide and oxygen to 16 patients in whom he was able to avoid anoxia by increasing the partial pressure of these agents. The validity of his conclusions subsequently was questioned by various investigators;[4–7] however, Faulconer, Pender, and Bickford[8] have concluded from their studies that the depth of anesthesia achieved with this technique is in direct proportion to the partial pressure of nitrous oxide. In addition, electroencephalographic changes were recorded which, in light of present understanding, corroborate the findings of Bert.

Dealing specifically with nitrous oxide and oxygen used alone and in combination with thiopental sodium, numerous publications have added much to this method of anesthesia.[9–18] Lundy, Adams, and Mousel, in 1939,[15] first described a technique of intravenous anesthesia for minor and major procedures in oral surgery. Subsequent modifications and improvements in techniques by Hubbell and Adams,[14] Bullard and Brockett,[12] and Thompson[18] and Royer[16] have contributed to the ease and efficiency with which anesthesia is produced in the oral surgical patient.

Additional knowledge was gained when, in 1955, Terpinas, Faulconer, and Royer[17] reported our observations in a series of patients who were undergoing oral surgical procedures. By means of a photoelectric earpiece, a continuous recording of arterial oxygen saturation was made in a group of patients who were receiving 5 different mixtures of nitrous oxide and oxygen. The partial pressure of oxygen corresponded to 13, 15, 17, 19, and 21% of the gas mixture. All patients received thiopental sodium. From these studies it was concluded that the margin of safety in respect to the occurrence of anoxia was markedly decreased as the partial pressure of oxygen decreased. In addition, arterial oxygen saturation during anesthesia produced by nitrous oxide-oxygen alone was very significantly below normal physiologic limits.

Nitrous oxide continues to be one of the chief inhalational anesthetic agents. Although it has weak analgesic properties, it has a wide range of application especially when it is supplemented with other anesthetic agents. A relatively recent clinical study along this line was conducted by Neff, Mayer, and Thompson[19] in 1950. They reported upon the use of meperidine hydrochloride in conjunction with nitrous oxide and oxygen in more than 2,000 cases. Small doses of meperidine hydrochloride were administered intermittently and intravenously, and use of the agent in this manner greatly enhanced the analgesic action of nitrous oxide.

For many years the field of general analgesia has been expanding steadily, and as newer drugs are developed and become available, methods and procedures also will change. More advanced and safer techniques are evolving, so that the risk to the patient during an anesthetic procedure is now minimal. Advances of this type will greatly facilitate the oral surgical procedures which must be done in the office, and at the

same time, application of the techniques of rapid induction of anesthesia, maintenance of lighter planes of anesthesia, and prompt recovery of the patient will become more nearly realized.

SOME NEWER ADVANCES

Dolitrone®. In 1953 Lundy[20] first became acquainted with, and launched the initial investigations of, a general analgesic agent known at that time as MRD-125. It was subsequently referred to as "Dolitrone®." In a group of 103 patients who were undergoing various oral surgical procedures, Dolitrone® was administered intravenously and was supplemented with nitrous oxide and oxygen. It was observed that once the patient had arrived at a degree of analgesia at which an operative procedure could be carried on, he was also able to respond to spoken commands. In addition, the patient experienced no sensation of pain and recovery was extremely prompt. Limited data were accumulated at this time in a comparison of the oxygen saturation of arterial blood during the use of thiopental sodium and during the use of Dolitrone®. Subsequent studies carried out with this agent, however, revealed that Dolitrone® would not remain stable for any length of time once it had been prepared. In addition, it also possessed the disadvantage of producing a moderate degree of thrombophlebitis upon occasion because of the high degree of alkalinity of the agent and the effect of the dependent position of the arm of the patient in the operative position required.

Promethazine hydrochloride. Recently attention has been focused upon a drug which has a broad application in surgery as well as anesthesia by virtue of its varied pharmacologic properties. It has been termed "promethazine hydrochloride" (Phenergan hydrochloride®) and chemically it is a member of the phenothiazine family. It is capable of exerting a powerful antihistaminic action as well as exhibiting sedative, antitussive, and antiemetic activity.[21] In our experience, promethazine hydrochloride has been employed as one of the premedicating agents, and we have observed that it has a definite potentiating action—which means that it is possible to use smaller quantities of analgesic and anesthetic agents when promethazine hydrochloride is also employed.

Ethylmethylglutarimide. An analeptic agent found to be of considerable value in the treatment of severe or acute barbiturate coma has also been found to be of distinct value in reducing the depth of thiobarbiturate anesthesia, and by so doing, hastening the recovery of the patient to a great degree. This drug has been called ethylmethylglutarimide (Megimide®). The agent is supplied for intravenous administration. It has been learned that it is not possible to indicate an appropriate standard dose; each patient requires a dose based upon individual evaluation.

Methyl-phenidylacetate hydrochloride. Still another agent which has been employed to antagonize the effect of depressant drugs is methylphenidylacetate hydrochloride (Ritalin hydrochloride®).[22] Clinically, it has been observed that Ritalin hydrochloride® will terminate, within a minute or so, the respiratory depression which occasionally follows heavy preliminary medication or the prolonged use of thiopental sodium. In a controlled study involving 370 patients, Gale[23] noted a statistically significant reduction in recovery time when this agent was employed to counteract depression of the central nervous system.

Levallorphan tartrate and others. In the management of respiratory depression associated with the use of narcotic agents as well as the newer synthetic analgesic agents, it is well to consider the application and use of one of the more recent analgesic antagonists, levallorphan tartrate (Lorfan tartrate®). Cullen and Santos,[24] in an uncontrolled study of 114 patients, observed the antidepressant effect of this drug when it was combined with levorphan tartrate (Levo-Dromoran tartrate®). Moreover, they suggested that it probably could be utilized beneficially as a premedicating agent in general anesthesia. In the appropriate dose, this agent is able to counteract the depressive effect of morphine, meperidine hydrochloride, Levo-Dromoran tartrate®, and alpha-prodine (Nisentil hydrochloride®). Of these 4 drugs, the last 3 have the greatest application in oral surgical practice. The supplementing of the thiopental sodium with nitrous oxide and oxygen and the intravenous administration of anyone of these agents and Lorfan tartrate® have developed a combined method of analgesia which is not only highly efficient but is also very flexible. Terpinas has used this technique of anesthesia on more than 1,000 patients in which a wide variety of procedures have been performed on an outpatient basis. In all these cases the postoperative response has been obtained in a period ranging from immediately to less than five minutes. Complications attributable to anesthesia usually have been minimal, so that the patient has been able to return home within a half hour to an hour after the operation.

Halothane. Recently considerable attention has been given to a new inhalational agent known as halothane. The basic experimental studies of this agent on animals were conducted in 1956 by

Raventós.[25] On the basis of his studies the author concluded that the agent possesses outstanding anesthetic qualities, including exceptional potency and easily reversible action. In all animals the induction of anesthesia was smooth and rapid and free of excitement, and recovery was equally so. The impression naturally was that in halothane an anesthetic agent was at hand which would not alter physiologic function and which, moreover, possessed the very qualities sought for in an ideal anesthetic agent.

Since the beginning, various authors throughout the world have contributed additional knowledge and experience in the use of this agent.[26–29] Goldman[26] described the technique of administration of halothane for oral surgical procedures. In his experience induction has been smooth and recovery rapid, and the method has been entirely suitable for outpatient surgical procedures. Side effects, such as nausea and vomiting, were said to be virtually nonexistent.

COMMENT

The particular use of one agent or another, as well as the technique of production of anesthesia, is governed by the magnitude and severity of the surgical procedure and many other factors, so that no single method of anesthesia is adequate for the multitude of oral surgical procedures to be performed. To this end, therefore, proper premedication as well as the administration of the anesthetic agents is, of necessity, indispensable, so that the ideal objective of minimal postoperative sequelae will be achieved.

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The Clinical Management of Peripheral Pain

Reflections On Twenty-five Years of Special Interest

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PERIPHERAL PAIN is used here in its clinical sense, that is, pain which arises in and is predominantly felt in the periphery or outer shell of the body, as distinguished from visceral distress. Peripheral pain may be primary, when its focus is in relatively accessible tissues, or it may be secondary to a deep focus.

Peripheral pain is one of the commonest complaints of patients seen in private practice and, in most instances, is quickly relieved by routine therapy or subsides with time. In other cases, however, the pain tends to persist or to increase. It is in reference to such cases that this article is written.

The majority of these persons were treated in private practice, with all the opportunities and limitations that this type of practice involves. A few were treated in military service and others in civilian hospitals in this country, South America, Africa, India, or Japan or Hong Kong.

TYPES OF THERAPY

Ultrasound, infrared light, short-wave diathermy, vasodilating agents, cold-producing agents, or injection of procaine-like solutions into trigger points or into nerve trunks or sympathetic ganglia are used.

This series does not include any patients found to have a visceral lesion directly responsible for the continuation of pain and the removal or treatment of which entirely removed the pain. These patients came from a variety of sources. Some were seen primarily, that is, before any medical therapy had been employed. Others were seen after medical, surgical, or manipulative therapy had been carried out without any or complete relief of pain.

Relatively few were of the hypersensitive types and races known to be overreactive to stimuli. Many were of the phlegmatic northern European races who tend to accept accidents and pain as routines in life. As an example, witness the Scandinavian farmer who walked into the hospital carrying over his arm all the skin torn off his abdomen, scrotum, and penis. His chief complaint was that the driver of the automobile, who brought him to the hospital, kept turning white and becoming syncopal.

Long-term follow-up of the subsequent course of these patients has been attempted. The population of rural Iowa tends to be relatively stable, as contrasted to city dwellers who tend to move every five years or oftener, according to statistics. Patients drive long distances to show results or write as to pain relief or recurrence. The aid of other physicians was enlisted so that follow-up records could be kept.

One reason for the long-term records was to determine the efficacy of various types of treatment. Another reason was to make sure that the diagnosis was correct. A third reason was to have exact techniques available if the injury were repeated or a pain syndrome recurred. Previous articles appearing in various medical journals have indicated some of the results of earlier work in this field.

OBJECTIVES OF TREATMENT

Ideal treatment of pain should be as simple and as specific as possible. It should involve little or no risk to the patient and should be economical in time, money, and the patient's tissues. The treatment course should cause little pain, should

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not damage the patient's adaptation to life, and should restore normal function, if at all possible. If a surgical procedure is necessary, it should not result in a defect that may predispose to future painful syndromes in the area.

Before any therapy for pain is carried out, a complete diagnosis should be attempted. This sounds axiomatic but is not. A truly "complete" diagnostic study occupies days to weeks of hospitalization and hundreds of dollars of expense. The majority of these patients received a complete physical examination, chemical and microscopic urinalysis, blood counts, sedimentation rate, blood serologic tests, and chest X-ray. In addition, studies of the amount of glucose, uric acid, and calcium in the blood were obtained when indicated. The radiologist interpreted the chest X-rays and further studies, including intravenous pyelograms, cholecystograms, upper and lower gastrointestinal evaluations, and roentgenograms of bones and soft tissues. Urologists, internists, orthopedists, otolaryngologists, and general surgeons were called in for consultation.

Do not attach a meaningless label to a painful syndrome because the pain happens to be localized to one area. Most patients with painful shoulders have been "diagnosed" as having bursitis or frozen shoulder, yet the pain actually arose in the cervical spine or the cervical sympathetics or from osteoarthritis of the shoulder joint. Pain arising from the thoracic spine is rarely recognized but is dismissed as intercostal neuralgia. Lumbar spine pain is usually termed a pain that is being caused due to a protruded intervertebral disk.

What pains should be treated? Useless pains should be treated, that is, pains that have outlived their usefulness or never were significant. To the patient and often to the physician, pain seems to be a warning of impending or actual tissue damage. As every physician knows, however, severe pains may arise from small external stimuli, and gross organic disease may become far advanced without any pain resulting.

For example, a woman falls on her outstretched hand. A fracture of the radius or phalanges may occur, but the outstanding symptom is severe pain which persists despite all conservative treatment. Because most such injuries return to relatively painless normal function, weeks and even months pass before it is realized that something unusual is going on. The fingers and hand may be swollen, glossy, tender, and weak. Injection of procaine solution into the stellate (cervical) sympathetic ganglion often relieves all the signs and symptoms dramatically. Such a condition may be concealed under one of these diagnostic terms: causalgia, sympathalgia, Sudeck's atrophy, posttraumatic osteoporosis or osteoarthritis, neuralgia, and psychogenic pain.

The shoulder-hand syndrome, persistence of pain in this area due to visceral disease, for example, coronary occlusion, may well be treated peripherally. When one considers shoulder and arm pains associated with a "frozen" or painful, nonmovable shoulder, it is well to remember that pain radiating from the cervical spine tends to spread over the upper and lower arm, rather than to remain in the region of the joint.

Injuries of the low back are exceedingly common, often persist and recur readily, and frequently respond well to procainization of trigger points in the interspinous ligaments, paravertebral muscles, and fascia. Sciatica can often be relieved by sciatic nerve block with the usual technique, which employs the posterior iliac spine and the greater trochanter as landmarks and with assurance that paresthesia is brought on by the needle point before the injection is begun.

Sharp trauma to the skin, a laceration or surgical incision being the same to the nerve endings, is occasionally followed by persistent pain recurring from a trigger point in the scar. Blunt trauma injury of subcutaneous tissues that sets up a deeper lying trigger point is far more common.

In such instances, an exquisitely tender area is usually easy to find, pressure upon which reproduces the pain. Interestingly enough, when this area is invaded with a needle, the patient often states, "That is the spot." Here again is the wisdom of the body, the localization of one trigger spot amid the vast central nervous system-computer-memory. Very frequently, the injection of a weak local anesthetic solution into this trigger point relieves the pain at once and forever.

Results of procainization. Several thousands of injections have been made to treat peripheral pain. More than two-thirds of the patients were relieved of pain dramatically. The others experienced good, partial, or no relief. Subsequent articles will detail the patients and the methods and results of treating painful conditions in each part of the body.

Are Anesthesiologists Losing Interest in the Management of Pain?

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THE FUNCTION of the anesthesiologist is varied. At one extreme he devotes all his time to the clinical management of patients under anesthesia, at the other to anesthesia research. Most anesthesiologists desire their function to be midway between these extremes.

The management of patients under anesthesia continues to improve. There are many pleasant, safe anesthetic agents from which to choose. There are also many refined techniques of administration. The ever-expanding surgical approach to disease, especially in cardiovascular and neurosurgical specialties, provides the anesthesiologist with an exciting challenge.

For those interested in anesthesia research, many sophisticated methods are available for monitoring the anesthetized patient. Superbly equipped anesthesia research laboratories are now conventional. This is a most desirable trend since all of us desire to administer anesthesia scientifically. Profound hypothermia and hyperbaric oxygenation techniques have provided another area for basic research in anesthesia.

A most important part of medical practice concerns the control of chronic pain caused by trauma and malignant diseases. The anesthesiologist is well qualified to treat patients with chronic pain and has contributed significantly toward solution of the problem. However, in recent years the anesthesiologist's interest in this subject seems to have been waning; a paper on the subject is rarely presented on an anesthesia program or in an anesthesiology journal. Endowments for basic research on the control of chronic pain are few. This lack of interest seems regrettable since thousands of patients have malignant disease, which usually is associated with severe pain. Also there is much trauma nowadays, which is likewise associated with chronic pain.

The present trend seems to be to treat pain with drugs. A great variety of drugs is available and many are effective, but most of them have definite limitations. They usually cause undesirable side effects, and the patient frequently develops a tolerance to them. It seems an imposition on the dignity of a patient to place him in a position of continually watching the clock to see when he can have more medication. Often, unpleasant personality changes occur in patients who have taken narcotics for a time. For example, patients with painful malignant lesions of the pancreas require narcotics. They become addicted and are hostile to their family and the nursing staff. After a successful splanchnic block, these patients become cheerful, are appreciative of the nursing service, and no longer request narcotics.

Much cancer research is being done. This is most desirable but it has added to the problem of pain control in some instances. Three recent patients illustrate this point. In each an abdominal exploration a year before had disclosed an inoperable malignant lesion of the pancreas. A splanchnic block was done for severe pain and a course of antineoplastic treatment was given. The patients were alive one year later but had to have another splanchnic block because of recurring pain.

In this era of so many scientific achievements, greater advances in pain control could be made. It is encouraging that some new techniques are being used. They include placement of needles aided by image amplification on a television screen, use of cryogenic methods to interrupt

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nerve transmission, and programming of pain control for computer analysis.

I hope the interest of the anesthesiologist in the control of chronic pain will be revived. The demand for such service is great and undoubtedly always will be. No one has maintained such an active interest in this subject, nor has anyone contributed so many improvements in the management of pain problems, as has the editor of this section on pain, Dr. John S. Lundy.

Current Literature on Pain . . .

BALL, H. C. J., PEARCE, D. J., and DAVIES, J. A. H.: *Experiences with therapeutic nerve blocks.* Anaesthesia 19:250-264 (April) 1964.

"In the last few years there has been an increasing demand for the establishment of pain clinics, particularly for the management of patients suffering from intractable pain due to malignant disease. . . . As anaestheticsts we have often been asked to help with these and other cases. . . . Patients have been referred to this Department by geriatricians, obstetricians, physicians, radiotherapists and surgeons. In each case adequate consultation, examination and investigation has been carried out as a preliminary to any therapy and notes have been recorded on a special form. . . . All patients have been treated whilst in hospital and although an attempt was made to continue "follow-up" in a special out-patient clinic this has now largely fallen into disuse and liaison is maintained through the clinician concerned. . . .

"It is most uncommon to obtain motor weakness with 7.5% phenol in iophendylate. . . . In cases which are difficult to assess it is often advisable to perform a diagnostic epidural or spinal block, using local analgesic drugs first. . . . Although intrathecal phenol blocks have also been used occasionally for benign conditions they are best reserved, in our opinion, as palliative procedures for malignant conditions. . . .

"The intrathecal block is best carried out without any special premedication or routine analgesic, the object being to assess as critically as possible the immediate response to the intrathecal injection. It is also best carried out on an operating table in an anaesthetic room or theatre because of the lighting and other facilities. A rigorous aseptic technique must be adhered to. . . .

"The remarkable thing is that other forms of sensation return very quickly and it is only the pain fibres which are blocked for any length of time. In some cases, however, the pain relief may not be altered for twenty-four hours. Afterwards the only complaint may be of some headache but with the disappearance of the severe pain other, more minor, aches and pains may become apparent and may require attention. . . .

"Blocks have to be repeated in many cases to provide more long-lasting complete relief of pain. . . . Of 51 cases, 17 required only one injection, 20 needed further intrathecal injections on a subsequent occasion while 6 required a total of three intrathecal blocks at intervals. . . .

"Most of our cases have had pain of a lumbo-sacral distribution resulting from pelvic neoplasms, or following excision of pelvic neoplasms, e.g., carcinoma of the rectum or cervix. The results in this group have generally been excellent. Results of treatment for malignant disease in other sites, particularly the abdomen, are much more variable. Many other nerve blocks may be required in the management of intractable pain due to malignant disease. In our series these have included Gasserian ganglion injection for Vth nerve pain, maxillary nerve block, brachial plexus block for upper limb pain and paravertebral thoracic block for chest wall pain from carcinoma of the lung.

"Sclerosing agents such as phenol have occasionally been used to provide permanent brachial plexus block in cases of malignant disease in an already useless arm. In other cases, where some motor power is still present and in cases of chest wall pain, we would now feel more confident in using cervical and thoracic epidural or intrathecal methods as outlined previously. . . .

"Spastic conditions may occur in many forms of neurological disease. . . . Initially we used 90% absolute alcohol for the intrathecal block. . . . We now use the hyperbaric solution of phenol in glycerine or iophendylate. . . . Following injection the patient is either kept in the lateral position for at least twenty minutes or otherwise postured in a slight semi-prone position so that the anterior roots are also affected. . . . In the spastic cases, remission occurred in 50% while there was considerable improvement in 37.5% and only moderate benefit in the remaining 12.5%. . . .

"The commonest cause of the sciatic syndrome is prolapse of an intervertebral lumbar disc, although other pathology has to be excluded. . . . Patients referred to us by orthopaedic surgeons have been given lumbar epidural injections of 20 to 25 ml. of 0.5% lignocaine solution with 100 mg. hydrocortisone or 80 mg. methyl prednisolone followed by straight leg raising or manipulation, when considered advisable, after an interval of ten minutes. The caudal route has occasionally been used. If large volumes (120 ml.) of solution are employed there is a risk of intra-ocular haemorrhage. . . . In the 47 cases treated epidural injection gave full relief to 25%; 18.75% were considered improved; 31.25% were only moderately improved for a short time while 25% gained no benefit at all. . . .

"Ischaemic states may affect any part of the body but particularly the brain, heart, kidneys and limbs. They include cerebro-vascular accidents, embolism, thrombosis, Raynaud's syndrome with or without scleroderma, arteriosclerotic or diabetic disturbances, thromboangeitis obliterans and injuries with impaired vascular supply. . . .

"In cases of peripheral ischaemia due to arterio-sclerotic changes or thromboses 66% needed no further treatment, although in a few incipient gangrene was present; lumbar sympathectomy was performed on 9% at a later date while 18% needed limb amputation and 7% had local excision of small gangrenous areas. . . .

"The advantages of epidural anaesthesia, either caudal or lumbar, in providing pain-free labour are well established. . . . Our experience is concerned with the abnormal conditions of labour, namely, eclampsia, pre-eclamptic toxaemia and cervical dystocia in which it is

felt that continuous epidural anaesthesia can be of the greatest benefit. . . . Of the 69 obstetric cases two thirds required epidural or caudal anaesthesia for primary cervical dystocia. In each case rapid dilatation of the cervix ensued and a live infant was delivered, usually by forceps delivery. The remaining cases of pre-eclamptic toxaemia or eclampsia were more difficult to assess, the majority having been subjected to heavy sedation initially. There was no maternal death amongst these cases, however. Co-existing foetal abnormalities or earlier death made the accurate assessment of foetal survival impossible."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

CASS, L. J., FREDERIK, W. S., and TEODORO, J. V.: *Pentazocine as an analgesic: clinical evaluation.* J.A.M.A. 188:112-115 (April 13) 1964.

"Pain is one of the most important protections that man has against the insults of his environment. . . . Pain is one of the manifestations of many diseases and, in itself, contributes nothing to the healing process while its presence may inhibit recovery. Although in illness and injuries of short duration this may not constitute a therapeutic problem, in the case of chronic or lengthy disease conditions, pain itself may be the limiting factor in the productivity and happiness of the individual. When pain is of long duration, potent analgesics which produce tolerance and dependence are usually contraindicated, especially in young people; this has limited the value and use of many of the most effective analgesics. . . .

"An interesting series of antagonists derived from the benzomorphan nucleus and possessing varying degrees of narcotic antagonistic activity in man has been studied by Harris and Pierson. One of the weakest antagonists in this series, the N-dimethyl-allyl analog of phenazocine (pentazocine), while it does not show analgesic properties in animals by use of the standard laboratory analgesic assay techniques, does demonstrate analgesic properties in man. There are indications that this compound is nonaddicting in both monkeys and in man. This investigation concerns the analgesic efficacy and the side effects of pentazocine in patients suffering from moderate to severe chronic pain. . . .

"Pentazocine in 40 mg. dosage approaches though is not equal to the analgesic effectiveness of morphine sulfate 20 mg. It produces basically the same side effects as morphine, but more severe and more frequent drowsiness. Pentazocine in 20 mg. dosage produces considerably fewer side effects than either morphine or pentazocine 40 mg., but still maintains a fairly high level of pain relief over a period of at least two hours. The delineation of an analgesic activity in this medication is potentially of special significance since it is a morphine antagonist derived from the benzomorphan nucleus and so far has been found not to produce or support tolerance or dependence."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

MILLER, D.S.: *Pain patterns due to entrapment of nerves.* Chicago Med. 66:1035-1037 (Dec. 14) 1963.

"The recognition of the so-called entrapment syndrome is relatively recent. A little more than ten years ago, the term entrapment began to appear to designate patterns of pain along peripheral nerves. . . . The term entrapment is not altogether apt. It should apply only when the nerves are actually trapped in tissue or by compression. The patterns of pain, however, may be the same when the cause is a viral inflammation. . . . Most entrapment neuropathies resolve themselves in time or under ordinary physical therapy, regardless of whether compression or inflammation is the cause. In intractable and persistent cases, surgical intervention is indicated in the forms of excision of the fibrous sheath over the nerve or muscle belly, neurolysis, excision of a nerve, or chordotomy or rhizotomy."

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COOPER, KENNETH and MOIR, J. C.: *Paracervical nerve block: a simple method of pain relief in labour.* Brit. M. J. 1:1372-1374 (May 25) 1963.

"The use of regional anaesthesia to relieve pain in the first stage of labour has generally been restricted to caudal and lumbar epidural anaesthesia. Excellent though these methods may be, technical difficulties detract from certain success in every case. A much simpler and more direct means of interrupting pain sensation from the uterus is to inject the anaesthetic solution into the loose cellular tissue at the side of the cervix. . . .

"A specially constructed guard-tube and needle is required. The essential feature is found in the injecting needle, which when inserted into the guiding-tube protrudes no more than 7 mm. . . . One hundred cases of paracervical block were performed on 94 women in labour. To the observer it was obvious that very substantial relief of pain was obtained in most cases. . . . Pain in the first stage of labour may be relieved for a period of one to two hours. . . . Complete or almost complete relief of pain was obtained in 71% of cases, and partial relief in a further 25%."

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FABIAN, L. W., HARDY, J. D., TURNER, M. D., and MOORE, F. J.: *A review of the present status of electronarcosis.* Anesth. & Analg. 43:87-96 (Jan.-Feb.) 1964.

"The purpose of this report is to describe the results of the use of electrical anesthesia with a group of 20 surgical patients and 5 human volunteers and to compare our results with those of other investigators. . . . Varying degrees of analgesia were obtained in all but 4 of the group. This analgesia ranged from complete lack of awareness in a few, to reasonably good analgesia at the operative site in most, to definite incisional pain comparable to poor local anesthesia in some. However, hypertension, tachycardia, and muscle spasticity were undesirable sequelae in every case. The results reported by other investigators in the field have been summarized and indicate similar findings in spite of certain modifications and refinements in methodology."

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HOOPER, R. L.: *Intravenous regional anaesthesia: a report on a new local anaesthetic agent.* Canad. Anaesthetists' Soc. J. 11:247-251 (May) 1964.

"A local anaesthetic compound with reduced toxicity would be a welcome addition to the anaesthetist's armamentarium, particularly with the revival of interest in intravenous regional anaesthesia. The clinical success enjoyed by lignocaine has led to the investigation of com-

pounds with a similar chemical structure. One such compound is a-n-propyl-amino-2-methylpropionanilide or Citanest. . . . The intravenous use of lignocaine for surgical analgesia in the extremities at the Lagos University Teaching Hospital (Nigeria) has been reported by Dawkins et al. In the clinical trial reported here, a similar method was used. . . . A total of 64 patients received intravenous Citanest. . . .

"The regional intravenous technique using Citanest was an effective means of producing surgical analgesia in the extremity. Citanest appeared to have a low toxicity. The only complication in the series occurred in a patient who had received 800 mg. of the drug, and who showed mild neurological symptoms. The use of 1.0 percent Citanest appeared to provide adequate analgesia and a volume of 20 cc. seemed to be a sufficient adult dosage. While the use of this volume-strength relationship provided a good margin of safety, the volume could be modified for paediatric or geriatric patients. Occasionally the distribution of analgesia was patchy. Since the veins are distended following the initial injection of the local anesthetic, a supplemental dose could be given if necessary. The language difficulty may have been partly responsible for the absence of reported subjective symptoms."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

MC DONALD, ROBERT, SHAW, MAURICE, and CRAIG, CECIL: *Effect of phenothiazines and analgesics, given during labour, on neonatal serum bilirubin.* Brit. M. J. 1:677, 1964.

"During labour many patients suffer extreme discomfort from uterine contractions; they become anxious about the outcome and are unable to relax. Such patients need analgesic and calming drugs. These must be safe for both mother and foetus, and be rapidly effective. Morphine and pethidine are well-established analgesics, but some patients require a tranquillizing drug as well. The combinations in use in the maternity unit of our hospital at the time of the trial were morphine with chlorpromazine and pethidine with promazine. It was decided to carry out a controlled trial to see if any of these drugs produced adverse effects on the serum bilirubin of babies born to mothers in the unit. . . . If a level of over 15 mg./100 ml. is taken to indicate hyperbilirubinaemia there were no cases of this in our series."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

MILLER, D. S.: *Bursitis and pain patterns.* Chicago Med. 66:567-570 (June 29) 1963.

"Diagnosis of bursitis of the shoulder joint may be baffling. The sudden onset is the first chief clue. The inexperienced would be wise to review the anatomy of the area before instituting treatment, particularly treatment by injections. . . .

"The subdeltoid bursa is the first of the painful areas in the region of the shoulder. Close to the subdeltoid bursa are two areas likely to produce a similarly painful shoulder: the acromioclavicular joint—superior to the subdeltoid bursa; and the bicipital tendon muscle-distal to the subdeltoid bursa. The subdeltoid bursa, the acromioclavicular joint, and the bicipital muscle may be thought of as The Big Three anatomic areas of pain. . . .

"Pain along the brachial plexus, from the fifth cervical to the first thoracic section, may also cause referred neuritis simulating bursitis of the shoulder. . . . Distally, Nature's entrapments of nerves by compression may provoke bursitis-like pain. . . . Viral infections of the soft tissues have been more frequently diagnosed in recent years. . . . Periarthritis seems to simulate subdeltoid bursitis more than any other disorder. . . .

"Graham and Rosen have written a succinct yet thorough review of the inclusiveness of the use of the term shoulder-hand syndrome to describe a variety of entities influenced by numerous associated disorders and circumstances. . . . Their recognition emphasized here is that this clinical entity may be a sequel to coronary heart disease; that myocardial infarction may provoke this syndrome of dysfunction and painful shoulders and referred neuropathy to the hand and intrinsic metacarpalphalangeal joints. . . . During recuperation from a heart ailment, treatment of the shoulder-hand syndrome must be cautious. A more vigorous program may be possible after recovery in the hospital."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

O'ROURKE, ROBERT, MANN, OSCAR, and HARVEY, W. P.: *Control of coronary pain by prevention of tachycardia.* J.A.M.A. 188:1005-1007 (June 15) 1964.

"It is a well-known physiological fact that the compromised circulation present in arteriosclerotic heart disease is further decreased in the presence of rapid paroxysmal rhythms. However, the clinical application of this fact is often overlooked in the treatment of so-called 'intractible coronary pain.' Some patients with coronary artery disease are completely free of anginal or coronary insufficiency pain except during episodes of tachycardia. In these patients treatment of coronary pain may primarily depend on prevention of paroxysmal rapid heart rates. . . .

"In evaluation of the patient with increasing anginal symptoms or with 'intractible coronary pain,' the existence of rapid paroxysmal heart action should be ruled out if possible. A careful history suggesting such an arrhythmia may lead to the correct diagnosis, and may at times be documented by an ECG taken during an episode of chest pain. Prevention of paroxysmal tachycardia can in turn result in prevention of coronary pain and possibly myocardial infarction."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

ROE, B. B.: *Are postoperative narcotics necessary?* Arch. Surg. 87:912-915 (Dec.) 1963.

"The routine liberal administration of narcotics to the postoperative patient is a deeply rooted surgical tradition based on the erroneous impression that devastating pain is the inevitable consequence of a major surgical procedure. . . .

"In more than 600 patients seen during a five-year period, postoperative administration of narcotics was sharply reduced from the usual dosage of 50 to 100 mg. to 4 mg. or less. Improved ventilation, earlier mobility, and less postoperative fear were noted by the attending staff, residents, and nurses who cared for these patients.

"The success of this regimen depends upon the cooperation of the patient which is obtained by the careful preoperative instruction in techniques of deep breathing and coughing. The positive pressure breathing apparatus is demonstrated to the patient and it is explained to him that his incision will be securely closed and cannot be disrupted by coughing or movement. He is told that

early mobility and ventilatory motion are essential for his safe and rapid convalescence. The amount of postoperative pain was not noticeably increased by this restrictive regimen. Larger doses of morphine were necessary in only a few cases."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

SHEFFIELD, W. E., KENNEDY, J. J., and DORNETTE, W. H. L.: *Clinical experiences with mepivacaine hydrochloride.* Anesth. & Analg. 43:192-198 (March-April) 1964.

"Mepivacaine hydrochloride . . . has been marketed recently in this country under the trade name of Carbocaine. . . . This study was begun in the spring of 1961 and was continued for approximately 17 months. We sought specifically to delineate 7 features of the compound's safety and effectiveness: (1) onset and duration of action; (2) quality of anesthesia; (3) comparative effects of the various concentrations; (4) effectiveness with and without epinephrine; (5) diffusability; (6) tissue compatibility and toxicity; (7) effects on the cardiovascular and central nervous systems. . . .

"A total of 1246 regional anesthesias for major and minor operations, therapeutic and diagnostic blocks, and intradermal injections were performed on 874 patients during a 17-month period by residents, interns, medical students, and staff members of the Department of Anesthesiology, City of Memphis Hospitals, and in the private practice of anesthesiology by one of us (WES). Mepivacaine solution in 1 and 2 percent concentrations with and without epinephrine was employed for these procedures. The toxicity, diffusibility, onset and duration of action, failures and complications were noted. No neurologic complications occurred and the incidence of toxic reactions was extremely low. In conclusion, we believe that the drug is valuable for the production of safe and satisfactory regional anesthesia for operative procedures."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

SANDMIRE, H. F. and AUSTIN, S. D.: *Paracervical block anesthesia in obstetrics.* J.A.M.A. 187:775-777 (March 7) 1964.

"We have been using paracervical block anesthesia in patients in labor for the past four years. . . . Obstetrical indications for use of paracervical block anesthesia include the following: (1) premature labor, (2) patients tolerating labor poorly, (3) cervical dystocia with posterior positions, especially if no disproportion is present, and (4) any laboring patient as a means of adding to the comfort of the patient. . . .

"We have used lidocaine hydrochloride (Xylocaine) lidocaine with epinephrine and mepivacaine hydrochloride (Carbocaine) and believe 2.0% lidocaine with epinephrine in concentrations of 1:200,000 to be the ideal agent. This will produce a duration of action of 1½ to 2 hours, whereas lidocaine alone and mepivacaine have a duration of action of about one hour. Recently we have been using 1.5% lidocaine with epinephrine in concentrations of 1:200,000 in place of 2.0% lidocaine with the same concentration of epinephrine. It appears that the 1.5% lidocaine provides results as good as the 2.0% solution. . . .

"Paracervical block anesthesia . . . was found to be a simple, safe means of adding to the comfort of the patient during the acceleration phase of the first stage of labor. Combined with pudendal block anesthesia, it produces satisfactory pain relief for the majority of laboring patients."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

STEINHAUS, J. E., BEVAN, WILLIAM, WEBB, S. C., and THOMPSON, W. R., Jr.: *Evaluation of analgesics by the rating of patient behavior.* Anesthesiology 25:64-70 (Jan.-Feb.) 1964.

"The purpose of this study was to evaluate the analgesic effect of four drugs on postoperative pain using ratings of patient behavior. For comparative purposes verbal estimates of pain provided by patients were analyzed in a similar manner. The four drugs selected for evaluation were meperidine, and three low potency analgesics—aspirin, acetophenetidin, and A.P.C. (acetylsalicylic acid, acetophenetidin and caffeine tablets, N.F.). . . . The selection of behavioral traits and construction of rating scales were made following a preliminary study of 10 patients who had clinically recognizable pain and who gave verbal response to that effect. . . .

"Using a double blind technique, four different drugs and a placebo were administered in random order to 65 patients with the qualification that 13 be in each group. . . . These ratings appeared to be more sensitive than the patient's verbal response which was determined concomitantly. A difference in the effectiveness of the analgesics tested was indicated."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

SINGH, N. P., KAPUR, B. M. L., MALHOTRA, K. K., and SACHAN, M. S.: *Evaluation of epidural sympathetic block in acute cerebral thrombo-embolic episodes.* Indian J. Anaesth. 10:216-223 (Nov.) 1962.

"Acute episodes of cerebral infarction either from thrombosis or embolism are quite commonly encountered in hospital and private practice. . . . From time to time attempts have been made to improve the cerebral circulation by use of vasodilators, anticoagulants, corticosteroids and sympathetic block. . . . The most effective method of improving cerebral blood flow is the inhalation of 5.7% carbon dioxide which produces seventy-five percent increase in normal persons. . . .

"When there is diminished blood flow, it is improved by inhibiting the sympathetic innervation which aids either by relieving the vasospasm or by increasing the flow through the anastomotic channels. . . . If blood supply can be promptly increased to the area of oedema and vasoconstriction relieved, the tissue reaction can be avoided and function of the brain can be reinstituted early. This is possible by sympathetic block and indicated only in cases of cerebral thrombosis and embolism while it is contraindicated in cerebral haemorrhage. . . .

"This study was undertaken to evaluate the efficacy of sympathetic paralysis by cervicothoracic epidural block in comparison to stellate ganglion block for acute cerebral thrombo-embolic episodes. This series of sixty-four cases of cerebral infarction was conducted at S.N. Medical College and Hospital, Agra, in 1959 and included only cases of cerebral thrombosis and cerebral embolism but not those of cerebral haemorrhage. There were 40 males and 24 females of varying ages. . . .

"Twenty-four cases selected at random were given sympathetic block, while the rest were treated by vaso-

dilator and anticoagulant drugs to act as the control group. . . . The immediate results were much more striking in cases of cerebral embolism than in those of cerebral thrombosis. . . . The cases of cerebral thrombosis also exhibited good results in comparison to the control group. Excellent results with complete recovery were obtained in three cases and good results with moderate recovery in nine other cases. . . . The results in control group of 40 cases were not remarkable. There were excellent results with complete recovery in three cases and that too in those of cerebral embolism, while good results with moderate recovery were noticed in another eighteen cases. . . . Continuous cervico thoracic epidural block has been suggested as a new and better alternative technique, more certain and devoid of many complications commonly accepted method of sympathetic paralysis by stellate ganglion block."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1964, vol. 63. Copyright by J. S. Lundy.

Book Reviews on Pain . . .

SEPTIC SHOCK: EXPERIMENTAL AND CLINICAL STUDIES, *by* HIROSHI HAYASAKA *and* JOHN M. HOWARD, *86 pp., Charles C Thomas, Springfield, Ill., 1964. $5*

"Dr. Hayasaka and Dr. Howard evaluate septic shock in terms of sesquestration of fluid in septic edema and toxic effects on the cardiovascular system as a result of exotoxin produced by gram-positive bacteria or endotoxin from gram-negative bacteria, or both. The peripheral vascular collapse which follows the toxemia of septic infection is characterized by initial vasoconstriction followed by or alternating with vasodilation, venous pooling of blood, and toxic action on the heart and adrenals in the very young and very old. The febrile patient has chills, pallor, tachycardia, hypotension, hypernea, and moist skin, but the underlying cause is obscured by ineffective antibiotic therapy. The stimulating experimental and clinical studies shed new light on a fatal syndrome in surgical practice." This is a statement by I. Newton Kugelmass, M.D., the editor of the series, "American Lectures in Living Chemistry."

"Septic shock has always carried a grave prognosis, particularly to the surgical patient. Because of the critical, multifaceted circumstances in which the complication develops, clinical observations have been of limited value and have almost always been confused by simultaneous therapeutic efforts. The resultant clinical progress has been limited.

"Meanwhile, many studies have been under way on the circulatory effects of bacterial endotoxin. Fewer investigations have concerned themselves with the circulatory effects of bacterial exotoxins or living bacteria. This monograph has been written with the purpose of providing an incomplete yet factual review of clinical and experimental observations as a foundation for future clinical investigation.

"The development of circulatory collapse in the course of sepsis marks a dramatic and often a dreadful event. In surgical experience, these patients are usually critically ill prior to this time because of a leaking anastomosis, postoperative abscess, intestinal gangrene, pneumonia, extensive burn, or gangrenous limb. The development of septic shock under such circumstances is often followed by death.

"Although the association of severe infection with vascular collapse was described a hundred years ago, greater attention has been focused on the pathogenesis of septic shock since World War I. Because of the multiplicity of circumstances, few analytical observations have resulted from the clinical experiences involved in this problem. As a result, most of the data which have been compiled center around studies of endotoxins, exotoxins, and other less clearly defined toxic factors involved in infections.

"The cause of hypotension in human infections has not been adequately studied. Endotoxin in the experimental animal causes a pooling of blood proximal to areas of vascular spasm or obstruction (splanchnic-portal and pulmonary beds) with a secondary decrease in cardiac filling and cardiac output. A generalized decrease in peripheral vascular resistance may occur late in this syndrome. Studies in the laboratory with endotoxin indicate that neither primary cardiac failure nor a major deficit in blood volume is responsible for the hypotension. Limited studies of infection by gram-negative organisms in man substantiate this finding.

"In addition to the overriding necessity to treat the infectious process, experimental studies suggest the value of certain adjuncts to therapy. Endotoxic shock in animals responds to treatment with aldosterone and, to a lesser extent, with hydrocortisone. Under the conditions of the experiments, this beneficial effect has been unequivocal.

"Adjuncts to the treatment of infections with gram-positive organisms or after the experimental injection of exotoxins have had very limited study. It is probable that the toxic effects will be more organism-specific than with the gram-negative organisms so that adjunctive therapy may have to be more specific. Data at present suggest that, somewhat like endotoxin, the toxins of staphylococci and meningococci cause peripheral pooling of blood, whereas the toxins of several of the clostridia, anthrax bacilli, and perhaps plague (P. pestis) result in increased capillary permeability with its secondary deficit in plasma volume.

"In each clinical application, adjuncts to therapy are adjuncts to operative drainage, debridement, antibiotic therapy, and the other fundamentals of established practice."

The authors state that septic shock has always carried grave prognosis, and they also point out the development of circulatory collapse. There is a discussion of the experiments, principally on animals, with endotoxins and exotoxins. There is a chapter entitled "Septic Shock," in which a description of the condition is attempted but not a definition of it.

The book is indexed, printed on good paper, and easily read, and an outstanding part is the bibliography of over 197 references. For those interested in the subject of shock, this book will be very illuminating.

JOHN S. LUNDY, M.D.
Seattle

Joseph E. Dahl

C. A. MC KINLAY, M.D.
Minneapolis



WHEN I WAS ASKED to prepare a profile of Joseph E. Dahl, the widely known and highly respected Minneapolis pharmacist, I felt pleased and honored, for he is a man whom I have known and appreciated for more than forty years.

He was born in Spring Lake, Minnesota, in 1890. His father was a schoolteacher and later became superintendent of schools of Isanti County. In later years he started a general store where Joe helped out after school, selling almost everything from cough syrups, castoria, and colic cures to groceries and wearing apparel. The cough syrups in those days contained morphine; although many samples were received for distribution, fortunately no one suffered any ill effects from them. The family later moved to Chisago City, consolidating with a similar store.

Joe's mother passed away of pneumonia when he was 13 years of age. There were an older and 2 younger brothers and a sister only 1½ years old. Four years later, the father remarried. Since Joe was no longer needed at home, he accepted a job in a Minneapolis drugstore. He opened the store at 6:30 each morning, 7 days a week, and worked until 9 o'clock one evening and 12 midnight the next. He averaged over one hundred hours a week. He soon realized he could not get sufficient sleep on that job, although he obtained wonderful experience. He assisted in making cough syrup in a 30 gallon barrel. An assignment he did not relish was fitting trusses. A more pleasant task was to fetch the horse and buggy at the livery barn for the physician whose office was above the drug store, and accompany him on sick calls. He felt he was serving the medical profession and creating goodwill as well.

On the advice of one of his fellow workers, he accepted another position which offered a slight raise to $35.00 per month—and a lot less hours. However, he had to sleep in the rear office to answer night calls and keep occasional intruders away. This store was in a good district and he delivered medications and other needed goods on a bicycle to many prominent people. He even installed gas mantles because electricity was not used by many. Lake Street was the end of the line in those days, and beyond that were mainly dirt roads.

After a few years a grandmother left a small inheritance to Joe. He had decided to stay in pharmacy, so he entered pharmacy college and, still working, spent all his spare time on studies. He soon passed the state board as assistant pharmacist, and a year later became a registered pharmacist. He could have stayed at his former pharmacy, but decided to try for a chance of serving in a more favorable pharmacy. Fortunately, he was accepted. There he earned $35.00 per week instead of per month, and had no late

C. A. MC KINLAY *is clinical associate professor emeritus, Department of Internal Medicine, University of Minnesota Medical School.*

evening work. Thus, he could devote a few evenings a week at the Y.M.C.A., enjoying the athletics in which he had always been interested.

The building in which his new position was located housed about 50 doctors, and his experience was most valuable. He prepared and sterilized arsphenamine (Salvarsan®) injections, which were then given intravenously by the gravity method of 250 cc. He assisted many physicians while they administered this preparation. Later Neosalvarsan® was developed which did not require neutralizing and could be given with a 10 or 20 cc. syringe. Also, he made up several hundred pills and powders daily. He developed techniques that enabled him to roll out 100 pills in six minutes. Infusion of digitalis was made every day and so were several batches of suppositories. White pine and wild cherry cough syrups were made by percolation. So in retrospect, this would seem more difficult than today when liquids are poured and pills are counted with less preparation.

After serving two years at this pharmacy, he was offered the opportunity of buying it. This store had been operating as the Andrus Building Pharmacy for nine years. His employer was opening a new similar venture on the fourth floor of the Syndicate Building. As he had surmised that the physicians would have to move out of the Andrus Building. This development happened, but Joe moved with most of the doctors to the Metropolitan Bank Building, this time on the ground floor. Three floors had been reserved for all the doctors from the Andrus Building. Only one of these men is still living and he retired years ago.

The new location proved good, but he had to deviate somewhat from his other location. He sold out to start a new venture, handling only biological, intravenous, and hypodermic medication, and offering all-night service. To handle the night service, he hired medical students, 4 of whom stayed until they graduated in medicine.

He developed a lucrative business in and out of the city. He remembers many a night and early morning when it was necessary to deliver oxygen and serums, making several bus and train connections for these emergencies. During this time insulin had been released for sale, and this proved to be a boon to this type of operation. Then the sulfonamides were introduced and serums were on the wane, so he gradually got back to the prescription business.

Fortunately, he found a store next to the Medical Arts Building and experienced two lean years while this was being built. It soon proved to be a good location. At this time he took in a partner. "After a few years I lost my lease to him and was forced to move to the Foshay Tower, which is one of our present spots." He also bought a pharmacy in St. Paul, which was sold after about ten years.

"To show my appreciation for the loyal support that I had enjoyed with so many of the medical profession, I thought an annual Christmas party would be a good idea. Starting with about 500 people, it finally grew close to 1,500. But after twelve years, problems developed and I was really sorry that this could not be continued."

All through these years he had been urged to carry some surgical and medical supplies. He finally yielded and now carries a complete line, which is separated from his 4 prescription pharmacies. He has 8 salesman representing him in 3 states.

On April 1, 1964, he celebrated his golden anniversary in business; for fifty-four years he had been a pharmacist. He has enjoyed wonderful health and has not missed a day because of illness in forty-seven years. He thinks "I can last another ten years."

"Times have changed and medications are entirely different—the items we used to buy in 10 gallon lots we now need only in pints. Dispensing then would seem more difficult, but now, with the multiplicity of items, our work is made harder.

"I am happy to say that I have stayed away from items that do not belong in a professional pharmacy. For this reason, I was invited to become a member of the American College of Apothecaries and am the first one in the Twin Cities to be accepted. Only 3 stores now have qualified."

Besides his interest in pharmacy, magic has been his hobby and "it has been a lot of fun." He is now serving as secretary for local International Brotherhood of Magicians.

"Spending over half of a century in the profession of pharmacy has not been a life of ease, but with God's help it has not been too hard to be of some service to a sick nation, with the good doctors carrying the heavy burden."

Throughout the fifty years that Joe Dahl has operated pharmacies, he has won a host of friends and admirers, such as Frank T. Cavanor, M.D., who says:

"I believe it was back in 1914 that I first met Joe Dahl. He was Joe to everybody, and I never heard an unfriendly word spoken about him. He was always studious and up-to-date in his business and I depended a great deal upon his knowledge of new drugs being brought out. The

Salvation Army, other organizations, and many poor people profited from their contact with him.

"In his role as magician he has brought entertainment to many. For many years his annual dinner to his friends and customers was a noted and eagerly awaited event. I have always been proud to have him as a friend."

As long as I have been a practicing physician, since 1921, I have known Joe Dahl. In all of those years, I have met no other man with a greater sense of integrity and responsibility or a more stable temperament and charitable attitude toward his fellow man. He is a notable combination of mildness and keeness, seriousness and alert good humor; a quietly dynamic, imaginative man who works throughout the busy days with a pleasant relaxed manner.

Joe and his wife, Elizabeth, who live at 6215 Halifax Avenue South, Minneapolis, were married March 10, 1915. They have a son, a daughter, and 2 grandchildren. For thirty five years Joe has been an ordained Elder in Knox Presbyterian Church. He is the type of man who puts his Christian beliefs to work daily in his business and professional life.

Those of us who were fortunate in being around during the era of the Dahls' Christmas dinners, when he and Mrs. Dahl entertained in a hotel ballroom, will never forget those gala evenings—the warm hospitality, the festive atmosphere, and the outstanding program of entertainment. Joe was just as much at home as master of ceremonies as he is at his pharmacy. And his dexterity as a magician is worthy of extended comment.

In 1962 he decided "to take the money which in past years was spent on Christmas parties, gifts or gadgets and invest it in the future welfare of our community by providing financial assistance to young persons seeking training in the nursing profession. We believe that this scholarship will encourage young women to continue their studies in a field that is of vital concern to the welfare of all of us—a field in which there is a recognized shortage of well-trained, qualified personnel." Mr. Dahl considers all his customers are participating in a superior endeavor.

Miss Carol Sue Fisher was the first recipient of the Joseph E. Dahl scholarships. She is using the fund to complete her work toward a Bachelor of Science degree in nursing at the University of Minnesota. She then plans to teach nursing.

A scholarship is given each year in the name of Mr. Dahl's customers. Therefore, when Miss Fisher reaches her senior year, there will also be junior, sophomore, and freshman recipients of scholarships. Thus, there will be 4 students in school at all times benefiting from the Joseph E. Dahl scholarships. What a noble gift to the nursing profession and the community!

The story of Joe Dahl is remarkable both personally and professionally. From early school days to the present he has been a hard worker. He has met the challenges that have come his way with energetic resourcefulness and his customary goodwill.

His professional career has coincided with the changing pattern of drug therapy and the dramatic development in chemicals and biologicals, when such basic therapy as insulin, the sulfonamides, and penicillin came upon the scene.

This continuous progression of new drugs placed increased demands on a pharmacist's professional responsibility, demands which Joe Dahl fulfilled with care and foresight. He and his pharmacies have always been symbols of highest quality in product and service alike. His specialized prescription pharmacies and now his center for medical and surgical supplies are significant features in the high-quality health service facilities of the Twin Cities and of the state.

Pharmacist, trustworthy businessman, host, magician, and good friend to man—that's Joe E. Dahl.

Book Reviews . . .

Cardiac Arrest and Resuscitation

by HUGH E. STEPHENSON, JR., *2nd ed., 501 pp., ill., C. V. Mosby Co., St. Louis, 1964. $15*

The author and his 10 contributors have enlarged on the original concept of cardiac arrest in the operating room and its environs to include in this volume every conceivable type of cardiac arrest short of exceptionally old age and advanced debilitating diseases. The subject is treated in every aspect, dealing first with a scholarly presentation of the history of cardiac arrest, resuscitation, and proceeding chronologically to the final brief chapter on predictions of the future. The most comprehensive discussions deal with the mechanism of cardiac arrest, the diagnosis, and the management. With the exception of a possible misstatement or proofreading error on page 93 dealing with adrenal corticosteroids in the treatment of anaphylactic reactions, the material is presented in easily readable fashion. The entire book is printed in clean, bold type with 1 or 2 larger, bolder offset subject headings on each page. Therefore, it is possible to literally read this book in scan fashion if one is looking for a ready reference or source material. This in itself should prove advantageous to third and fourth year medical students, as well as house officers of any moderate to large-sized hospital.

What of the general practitioner who makes up the bulk of the medical book readers the world over? What does he care of the comparison of direct and indirect current defibrillators? Isn't it quite enough they master the fact that there is an electrical shock machine for the treatment of ventricular fibrillation if the diagnosis can be established? This book is not a primer for the general practitioner, but it is a must for the doctor who is involved in establishing a cardiac emergency unit in his hospital. As soon as any physician becomes involved in a hospital scheme for treating cardiac emergencies he must acquaint himself with the machinery, electronic or otherwise. He cannot turn to electronic catalogues because these are definitely tilted in one direction, but he can use Dr. Stephenson's book as a veritable Bible. Not only is the machinery discussed but also the essentials of establishing a cardiac emergency unit in all details.

The reviewer objects to the obsession with time in cardiac emergencies. It would be preferable that the nurse on page 232 skip over step 1 which orders her to note time, and proceed to all the other measures, noting time if possible. It is important to save time, not to note it, for who is to say when the oxygen transport to the vital organs became inadequate—regardless of the clock on the nurse's desk.

The book includes the best summary of cardiac drugs that the reviewer has encountered. There is included a two-page protocol for quick operating room use if and when there is a divergence of opinion on the specifically indicated drugs during the one or two hours involved in a cardiac resuscitation. This protocol in itself might well put the book on every anesthesiologist's shelf.

The medicolegal aspects of cardiac arrest make good detailed reading—in essence pointing up the problem but exhorting the physician to do all in his power quickly and not to use precious moments calculating the legal risk. The author of this section urges a "malpractice program" rather than the usual malpractice insurance but does not elucidate to any degree. He hints at governmental interference which to this reader is evidence enough for quick and concerted action on the part of all medical societies.

The closing paragraphs would indicate that the author looks for an exciting new "breakthrough" in the broad field of cardiac resuscitation and prolonged reconstitution. In essence, Dr. Stephenson has given us a comprehensive book on a most vital subject in which he and his contributors have drawn on no less than 1,800 separate authors the world over, both up-to-date and from the distant past. He presents the problem, treats all aspects, and predicts a brighter future.

SAMUEL W. HUNTER, M.D.
St. Paul

Accident Injuries of the Conjoined Femur

by JACOB KULOWSKI, *294 pp., ill., Charles C Thomas, Springfield, Ill., 1963. $12.50*

This is a rather unique book because the author has been intensely interested in the incidence, cause, evaluation, and prevention of automobile injuries for many years and has produced numerous fine exhibits on the subject in many orthopedic meetings. He has chosen the femur and its associated structures as a central area receiving major injury from automotive impact.

This book is based on an analysis of 287 automotive injuries on the femurs of occupants of four-wheel motor vehicles plus 65 miscellaneous injuries produced by a variety of vehicles, pedestrian injuries, and falls. No explanation is made for the combination.

The author then takes the reader through a somewhat devious route of the various components of the injury complex, including constant and unconstant exogenous factors, multiple injury patients whom the author terms "once-twice-thrice injured persons," and their state of health prior to the accident.

There is a good deal of history and some philosophy throughout the book. Free use is made of the experience of other surgeons, past and present, in discussing dislocations and fracture dislocations of the hip area. The author's statistical analysis of individual problems is not extensive. For example, he analyzes 19 posterior fracture dislocations, 11 of which were treated conservatively and 5 by operative reduction. He reports only 2 patients with associated fractures of the femoral head, 1 of whom died of "relentless shock."

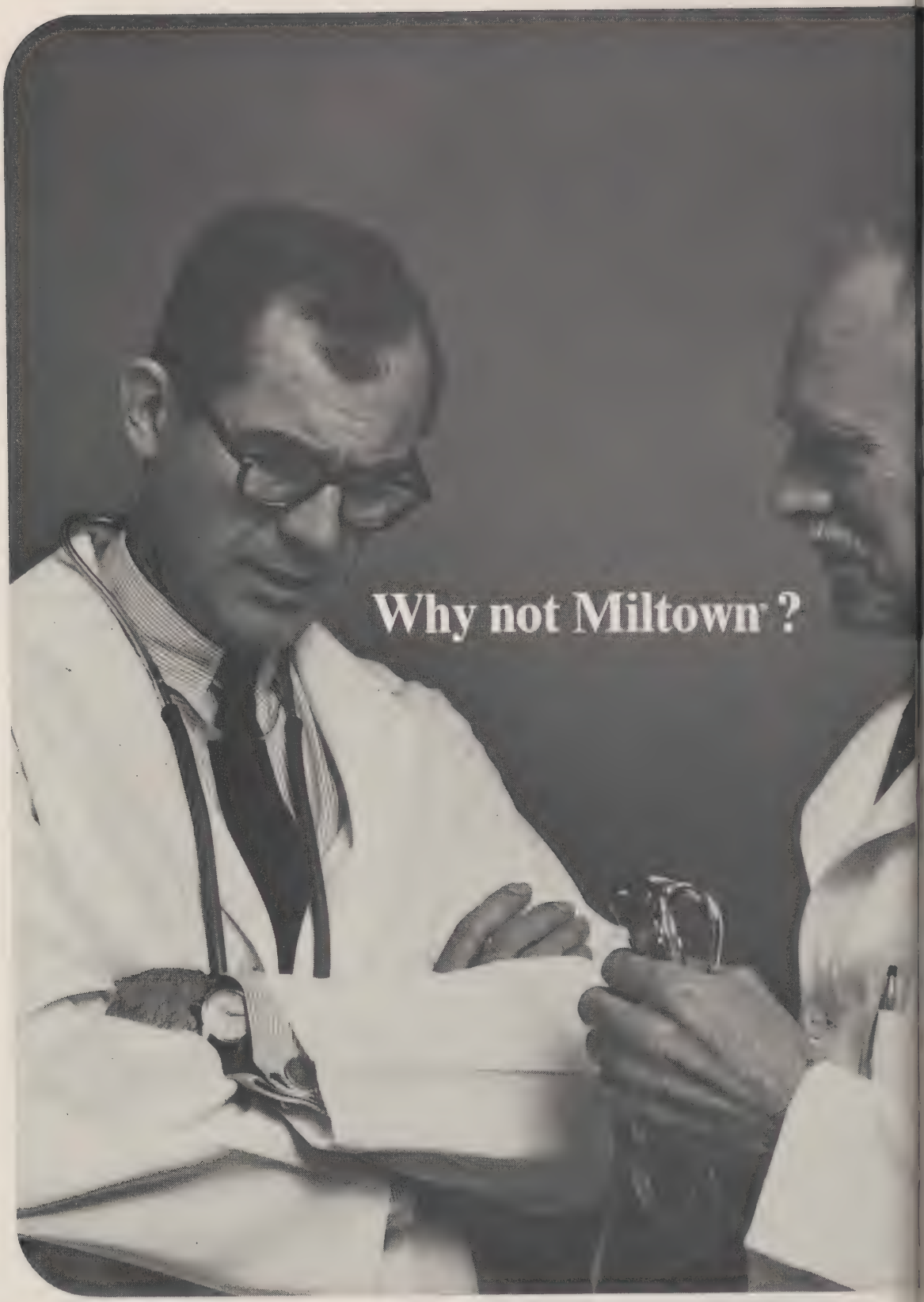
The same use of a bibliography is made of injuries to the knee region.

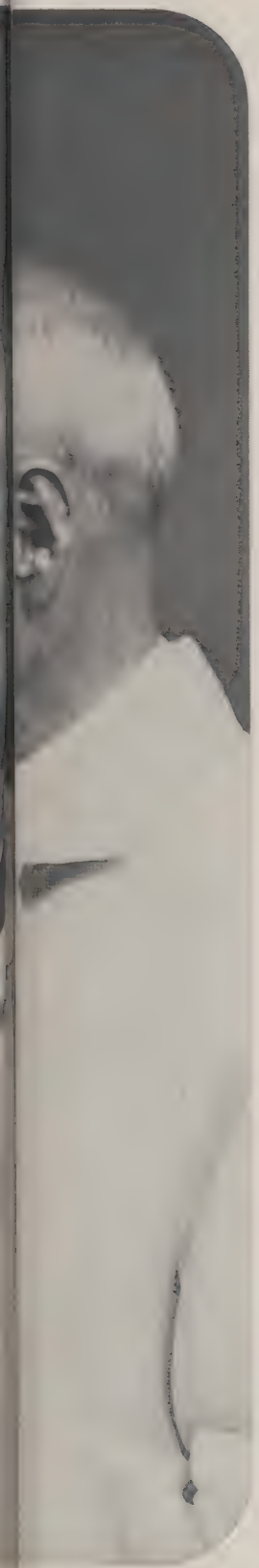
This is an interesting book, full of photographs of injuries and crashed automobiles. It is more informative on the causes and nature of associated injuries than on their management.

The final chapter on bioengineering problem of prophylaxis includes interesting comments on the value of various types of seat belts.

In general, this is a book of interest but contains a

(Continued on page 18A)


Why not Miltown ?



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Contraindications: Previous allergic or idiosyncratic reactions to meprobamate or meprobamate-containing drugs.

Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Usual adult dosage: One or two 400 mg. tablets three times daily. Doses above 2400 mg. daily are not recommended.

Supplied: In two strengths: 400 mg. scored tablets and 200 mg. coated tablets.

Before prescribing, consult package circular.

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(Continued from page 15A)

great deal of information which is fairly well known to the orthopedic surgeon and others dealing with trauma. Perhaps it is of greatest benefit to the medical student and general practitioners.

JOHN H. MOE, M.D.
Minneapolis

Melanotic Tumors: Biology, Pathology, and Clinical Features

by JOSEPH N. ATTIE *and* RENE A. KHAFIF, *346 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $12.50*

The uncertainty and confusion about melanoma, owing to the relative rarity of the disease and its eccentricities, the controversial nomenclature, and the variety of surgical procedures employed in its treatment, have been recently compounded by various claims from numerous chemotherapeutic drugs and techniques. An orderly and authoritative presentation of the subject would be, therefore, particularly timely and welcome.

"Melanotic Tumors," however, is basically a collective review with 500 references written by 2 surgeons, covering many aspects of the subject from the biochemistry of melanin and the embryology of the melanocyte to the pathologic and clinical aspects of melanotic tumors. The illustrations are in black and white, some of poor definition and with occasional errors (legend of figure 75, page 213), and are mostly reproductions of other authors' work. Colored reproductions, a sine qua non, in the discussion of differential diagnosis of pigmented lesions, are not used. The last chapter on treatment and end results occupies one-third of the book and covers in some detail various surgical and recent chemotherapeutic techniques. At the end of this chapter, the results of various reported series are presented and compared. This comparison, however, is not entirely valid since it is difficult to compare five-year survival figures in groups of patients whose stage of disease is unknown.

Definition of terms, staging of the disease, and particularly interesting clinical problems such as ocular melanoma and inadequately treated or recurrent melanoma have been given too little attention.

The lack of authoritative opinion which is sensed throughout the book is consistent with the fact that reference to the authors' personal work is made only once in the legend of a figure (figure 74, page 211), and this not in reference to melanoma.

As a collective review this book has largely succeeded in its purpose but it is lacking as a rational guide in the practical management of this disease.

A. N. PAPAIOANNOU, M.D.
New York City

General Principles of Blood Transfusion

edited by MAX M. STRUMIA, WILLIAM H. CROSBY, JOHN G. GIBSON II, TIBOR J. GREENWALT, *and* JULIUS R. KREVANS, *40 pp., ill., J. B. Lippincott Co., Philadelphia, 1963. $2*

This book is divided into several sections, the first dealing with general considerations of blood transfusions and the relationship of the clinician and the transfusion service. The author discusses the length of time that blood



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should be kept in the blood bank and when whole blood and packed red cells or plasma should be given. Section II consists of the clinical considerations. The author discusses measurement of blood volume, relationship of hemoglobin concentration and hematocrit value in regard to severe hemorrhages with shock, and plasma as a volume expander.

This book is especially valuable to surgeons to help them anticipate the amount of blood necessary for surgical procedures. The rate of transfusions is very important. I think doctors often are inclined to give the transfusion either too slow or too fast, depending on the condition of the patient.

One of the factors that has become very important in the last few years is the replacement of the clotting factors in the plasma and the blood. We have factors I, II, V, VII, VIII, IX, XI, and XII. This book discusses, in a very abbreviated form, but to the point, the treatment of specific hemorrhagic conditions such as thrombocytopenia, fibrinogen deficiency, classical hemophilia, and factors IX, XI, V, and VII deficiencies.

Section III discusses conditions that require large and small transfusions, exchange transfusion for circulatory crisis or hyperbilirubinemia to prevent kernicterus, anemias due to hemorrhage or hemolytic disorders, and transfusions for poisoning, leukemia, and autoimmune hemolytic anemia.

Section IV on special procedures has to do with pressure transfusions, warmed blood, autotransfusions, and cross transfusions.

Section V has to do with serologic considerations. It is important that the antibodies and the autoagglutinins be determined so that precautions may be taken when one gives several or single transfusions.

Section VI discusses the allergic reaction and bacterial contamination from transfusions, plus the hemolytic reactions and the renal insufficiencies that result from blood incompatibility.

Last is the section on legal considerations. The liability for improper and incompatible blood is discussed, as well as contaminated blood with homologous serum jaundice, malaria, syphilis, or other infectious diseases, and the injury to the recipient that may result from the blood. Also discussed was the subject of injuries to the blood donor from withdrawal of blood for cross-matching and preparing him for treatment with blood transfusions.

This is a very well written book and is short and easy to read.

E. N. NELSON, M.D.
Minneapolis

Principles of Public Health Administration

by JOHN J. HANLON, *4th ed., 719 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1964. $11.50*

This fourth edition brings up to date the latest advances in public health administration that only the distinguished author with his vast experience can do. In some of the chapters new material has been added, for example: maternal and child health activities, chronic diseases and adult health, mental health, public health, the private physician, and medical care.

In this ever changing society in which we live, public health must assume a more responsive role in meeting the ever increasing noncommunicable health needs of the people. Yet it cannot relax any of the time proven mea-

(Continued on page 20A)

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FREE PARKING

(Continued from page 19A)

sures to control environmental and medical contagion. Urbanization, changes in industrial technology, more rapid increase in the older population, and greater awareness of mental disturbances will demand greater effort and "thoughtful imagination" of all public health workers if they are to address themselves "to the solution of the fascinating challenges of the future . . . ."

This book is designed to be a stimulating textbook, reference, and guide to all public health workers who naturally wish to retain the successful health controls of the past, to cope with current day problems, and to pioneer into the future. Dr. Hanlon presents his material in an exciting manner with authority that comes from his rich experience. The book is highly recommended to both practitioners and students of public health, medicine, nursing, pharmacy, dentistry, and all other related fields.

HILBERT MARK, M.D.
Toledo

A Guide to Learning Fluid Therapy

by DANIEL C. DARROW, *280 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $9.75*

Proper fluid and electrolyte therapy is essential in many medical and surgical conditions. With increasing knowledge concerning intra- and extracellular fluids, physicians have an obligation to keep abreast of developments in this field.

This book by Darrow contains practically all of the available scientific information concerning body fluids. Darrow himself is probably the outstanding authority on the subject. However, it is no easy shortcut to therapy. The practicing physician unaccustomed to thinking in terms of milliequivalents, mols, and millimols will find much laborious reading, but those willing to spend time in concentrated study cannot help but learn much of value in understanding and treating their patients.

Specific chapters on diarrhea, fluids for surgical patients, diabetic acidosis, edematous states, adrenal steroids, and body fluids are among portions of the book which are of particular interest.

LAURENCE G. PRAY, M.D.
Fargo

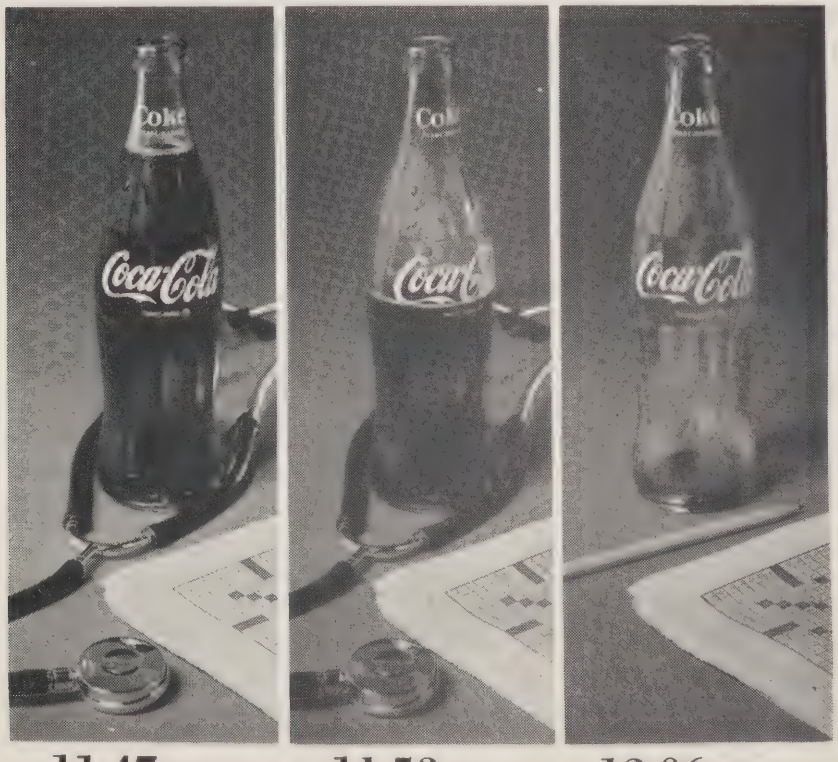
NEW BOOKS RECEIVED

Career Training in Child Psychiatry by OTHILDE KRUG, executive editor, 260 pp., ill., American Psychiatric Association, Washington, D. C., 1964.

Photographic Illustration for Medical Writing by DONALD J. CURRIE and ARTHUR SMIALOWSKI, 116 pp., ill., Charles C Thomas, Publisher, Springfield, Ill., 1962. $7.50

Industrial and Traumatic Ophthalmology by ARTHUR H. KEENEY, HEDWIG S. KUHN, RODERICK MACDONALD, JR., FRANK W. NEWELL, JOSEPH F. NOVAK, RALPH W. RYAN, and LORENZ E. ZIMMERMAN, 321 pp., ill., C. V. Mosby Co., St. Louis, 1964. $14.50

A Doctor Discusses Pregnancy by WILLIAM G. BIRCH and DONA Z. MEILACH, 114 pp., ill., Budlong Press Company, Chicago, 1963. Complimentary copies will be sent to physicians requesting same on their professional stationery by writing to the Professional Service Department of Budlong Press Company.



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News Briefs . . .

North Dakota

DR. JOHN J. MCLEOD is the thirteenth chief of staff and president of the executive board of St. Michael's Hospital in Grand Forks. Other officers are Dr. William P. Keig, Jr., vice-president, and Dr. John H. Graham, secretary.

A 1947 graduate of Marquette University School of Medicine, Milwaukee, Dr. McLeod has been a member of the hospital staff for the past nine years. He interned at St. Mary's Hospital, Duluth, and was a Fellow in orthopedics at the Mayo Foundation.

* * * *

DR. E. KEITH BORDEN is now associated with the Dakota Clinic, Fargo, in the department of internal medicine. A native of Montreal, Dr. Borden received his medical degree from McGill University in 1956. He interned and spent two years in residency at Ohio Valley General Hospital, Wheeling, W. Va., plus a two-year residency at Montreal General Hospital and a year at the Cleveland Clinic. Dr. Borden also served as a consultant in internal medicine with the Canadian Army.

* * * *

DR. CLIFFORD J. KLEIN has been elected president of the Valley City Medical Association. A general practitioner, Dr. Klein received his medical degree in 1949 from Stritch School of Medicine of Loyola University, Chicago. He is a member of the American Academy of General Practice. Dr. Milton O. Berg was named vice-president of the association and Dr. John Wm. Goven, secretary. The three physicians also serve as officers of the medical staffs for the city hospitals.

* * * *

DR. JOHN JAMIESON has become associated with Dr. Eoin Harvey at the Tioga Clinic. A 1950 graduate of Glasgow University, Scotland, Dr. Jamieson interned at hospitals in Scotland and England.

* * * *

DR. C. ROBERT MILLER, a general practitioner of Bottineau, has been elected president of the Lake Region Medical Society. Dr. Miller is a 1960 graduate of the University of Nebraska College of Medicine and a member of the American Academy of General Practice. Other new officers of the society are Drs. David A. Rinn, Cando, vice-president, and Louis F. Pine, Devils Lake, secretary-treasurer.

* * * *

DR. ANDREW C. SAWCHUK is the new chief of staff at St. Joseph's Hospital in Dickinson. Dr. Sawchuk, a general surgeon, was graduated in 1951 from Queen's University Faculty of Medicine, Kingston, Ontario. Additional staff officers elected are Drs. Walter C. Hanewald, vice-president, and Donald James Reichert, secretary.

* * * *

DR. ROBERT L. GESTON has been elected chief of the medical staff of St. John's Hospital, Fargo. Dr. Geston, a general practitioner, is a 1960 graduate of State University of Iowa College of Medicine and a member of the American Academy of General Practice. Also elected to office were Drs. Gordon Bristol Magill, vice-president, and Henry James Weyers, secretary-treasurer.

* * * *

A POSTGRADUATE MEDICAL RESIDENCY program will be established at the University of North Dakota under a

(Continued on page 22A)

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NEEDED—General Physician—Family Internist by four-man group in growing rural program in West Virginia. Modern clinic facilities, regularly visiting specialist consultant staff, scheduled training and vacation periods, foundation sponsorship, no investment required. Starting net income range $14,000-$18,000 depending on qualifications. Reply Box 22, c/o Journal Lancet.

DOCTOR for general practice work in established clinic with another Doctor. Beginning salary $1500.00 per month with opportunity for partnership after one year. Progressive W. N. Dak. town with 30 bed hospital. Reply Box 25, Journal Lancet.

WANTED LOCUM TENENS: One month, G.P. or General Surgeon. Minnesota License. Northern Minnesota small town practice. Handsome remuneration. For January, February, March or April. Reply Box 27, c/o Journal Lancet.

MEDICAL CLINIC BLDG. FOR RENT—Wonderful opportunity for new group. Located at 36th and Noble Ave. No. in No. Suburban Minneapolis. Deluxe Bldg. Unlimited parking—5 minutes to two hospitals. Available June 1. Inquire at Noble Drug, JU. 8-9449 or LI. 5-3505.

WANTED—General practitioner or physician interested in internal medicine to join rural clinic in N.W. Minn. Excellent hospital facilities, good school, churches, golf course, fishing and hunting. Write Box 28, Journal Lancet.

WANTED—Younger or older General Practitioner who is tired of solo practice for association with 15 man midwest clinic in town of 30,000. Two Generalists now on staff. We can offer a more comfortable but adequately compensated Family Practice with accessible consultation and off-time coverage. Write Herbert H. Kersten, M.D., Fort Dodge, Iowa.

WANTED DOCTOR to locate in city of 1,000 in Red River Valley of North Dakota. Fine modern medical building. New 60 bed Nursing Home to be completed September 1st. Financial help and housing available. Reply to Harley Nash, Sec'y., Hatton Medical Center, Hatton, N.D.

WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED—Young (30-35) general surgeon, Board eligible or qualified, to associate with group of general practitioners, North Dakota. Offering generous salary and early full partnership. Reply Box 29, c/o Journal Lancet.

NEWS BRIEFS

(Continued from page 21A)

recent agreement between Quain and Ramstad Clinic of Bismarck and the State Board of Higher Education. Approved residencies will be offered in internal medicine, radiology, and surgery.

While the agreement involves Quain and Ramstad Clinic, Bismarck Hospital, and the radiological section of St. Alexius Hospital, the program will be open to any other group or hospital.

The program will be administered through the university's medical school with the clinic contributing all but some minor administrative costs. Dr. Lloyd S. Ralston is to be Quain and Ramstad clinical director of the program.

* * * *

DR. JAMES B. MOFFETT has joined the staff of Quain and Ramstad Clinic and will serve in the Department of Internal Medicine. A native of Missouri and a 1946 graduate of Washington University School of Medicine, St. Louis, he interned at Baptist Memorial Hospital in Memphis, Tenn. A residency in internal medicine was completed at U. S. Army Tripler General Hospital in Honolulu, followed by a residency in pulmonary diseases at Fitzsimmons General Hospital, Aurora, Colo. Dr. Moffett recently retired from the army after twenty years of service.

* * * *

DR. ROBERT B. TUDOR was reelected chairman of the board of trustees at the annual meeting of the Bismarck Medical Foundation, a subsidiary of Quain and Ramstad Clinic. Dr. Tudor, a pediatrician, is a 1938 graduate of the University of Minnesota Medical School. He is a member of the American Academy of Pediatrics, the American College of Physicians, and the American Thoracic Society.

The foundation named Dr. Marlin J. E. Johnson vice-chairman and Drs. Clifford H. Peters and Johnson were reelected to three-year terms on the board.

Minnesota

DR. CLINTON C. RHODES has joined the staff of the Itasca Clinic in Park Rapids. Dr. Rhodes is a graduate of the University of Minnesota Medical School. He served his internship at Ancker Hospital in St. Paul.

* * * *

NEW PRESIDENT of the Range Medical Society is Dr. Charles B. Will. The International Falls physician is a 1939 graduate of the University of Minnesota Medical School and a member of the American Academy of General Practice. Other officers are Drs. H. Wayne Johnston, Virginia, vice-president; Fredric L. Mast, Chisholm, secretary-treasurer; and Roger W. Brockway, Grand Rapids, president-elect.

* * * *

DRS. JAMES B. FLINN and WILLIAM B. EILERS of Cairns Clinic, Redwood Falls, have arranged to maintain some office hours for general practice in Morgan. They will occupy the former office of Dr. William E. Johnson, who has joined the staff at St. Cloud Veterans Administration Hospital.

* * * *

DR. LLOYD C. DEMARAIS has been elected president of the Hibbing General Hospital medical staff. Dr. DeMarais, a surgeon, was graduated from the University of Wisconsin Medical School in 1952.

NEWS BRIEFS

DR. WESLEY W. SPINK has been named to a new medical advisory board that will aid the Federal Food and Drug Administration in its safety program for drugs and therapeutic devices. Dr. Spink, professor of medicine at the University of Minnesota, was born in Duluth and graduated in 1932 from Harvard Medical School. He served his internship at Boston City Hospital and was a resident physician at the Thorndike Memorial Laboratory. Dr. Spink, a world authority on infectious diseases, is a past president of the American Society for Clinical Investigation, The Central Society for Clinical Research, and the American College of Physicians.

* * * *

DR. CHARLES WM. MAYO of Rochester, emeritus member of the Mayo Clinic staff, has received the Distinguished Service Award of the American Society of Abdominal Surgeons. The presentation, made in New Orleans at the society's sixth annual clinical congress, cited Dr. Mayo's "long and distinguished career in surgery." Dr. Mayo is the fifth recipient of the award.

* * * * *

DR. LLOYD A. WHITESELL, JR., a general surgeon, has opened an office in Chanhassen. A staff member of St. Francis Hospital in Shakopee, Dr. Whitesell received his medical degree from the University of Minnesota in 1933. He interned at Charity Hospital of Louisiana at New Orleans, and practiced for one year at Huey P. Long Charity Hospital in Pineville, La., prior to serving with the Army Medical Corps in Korea. Dr. Whitesell is a member of the International College of Surgeons, the American Academy of General Practice, and the Aerospace Medical Association.

DR. DONALD ARTHUR BOLT has opened an office in the PBC Medical-Dental Center, Brooklyn Center. Dr. Bolt was formerly chief of general surgery at the army's Madigan General Hospital, Tacoma, Wash. Originally from Montevideo, he was graduated from the University of Minnesota Medical School in 1955. He interned at Walter Reed General Hospital where he also received specialty training in general surgery. Dr. Bolt, recently discharged from the army, is a diplomate of the American Board of Surgery.

* * * *

DR. RICHARD E. OLSON has joined the partnership of the Valley Medical Clinic at Jordan. He has been associated with the clinic during the past year. A general practitioner, Dr. Olson received his medical degree from the University of Minnesota in 1960.

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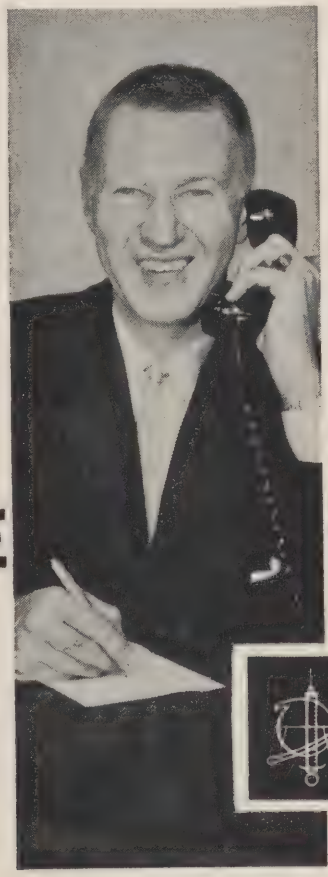
DR. LINNEUS G. IDSTROM has been reelected president of the medical staff of Swedish Hospital, Minneapolis. A resident of Edina, Dr. Idstrom specializes in pulmonary diseases. He is a 1939 graduate of the University of Minnesota Medical School and a member of the American Board of Radiology. Other staff officers reelected were Drs. George H. Marking, Minneapolis, president-elect, and Willis M. Duryea, Jr., Edina, secretary-treasurer.

* * * *

DR. ANN S. GOLDSTON will be associated with the Austin Clinic, Department of Pediatrics, on a three-day-a-week schedule. Following graduation in 1956 from the Medical College of Virginia, Dr. Goldston interned at Norfolk General Hospital in Virginia. She is a former Fellow in pediatrics of the Mayo Foundation.

(Continued on page 24A)

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NEWS BRIEFS

(Continued from page 23A)

DR. GORDON E. LEE has been reappointed chief of the medical staff of Glenwood Community Hospital. Dr. Lee is a general practitioner. He received his medical degree in 1953 from the University of Minnesota. Also named at the annual staff meeting were Drs. Berton A. Kolp, vice-chairman, and Rosemary R. Frear, secretary-treasurer.

* * * *

NEW CHIEF OF STAFF at Sanford Hospital in Farmington is Dr. Samuel P. McDaniel, Lakeville general practitioner. Dr. McDaniel received his medical degree from Emory University in 1916 and is a member of the American Academy of General Practice. Other staff officers elected were Drs. Jurgen J. Moller, vice-president, and Warren L. Kleinsasser, secretary.

* * * *

AT THE ANNUAL MEDICAL STAFF MEETING, doctors at Worthington Municipal Hospital elected Drs. Arthur F. Amick, president; Edward P. Seisler, vice-president; and Bhasker J. Desai, secretary-treasurer. Dr. Amick is a graduate of Harvard Medical School. Dr. Seisler received his M.D. from Hahnemann Medical College and Hospital of Philadelphia and Dr. Desai was graduated from the University of Bombay.

* * * *

DR. DANIEL R. GOLDISH has been installed as chief of staff at St. Mary's Hospital, Duluth. A member of the American Academy of General Practice, Dr. Goldish received his medical degree in 1932 from the University of Minnesota. Other officers include Dr. Phillip V. Halliday, secretary, and Dr. Frederic T. Becker, chief-elect for 1966.

* * * *

DR. HUGH D. THORFINNSON, a graduate of the University of Illinois College of Medicine, has been elected chief of medical staff at St. Ansgar Hospital in Moorhead. Dr. D. L. Carlson is the new vice-president of the staff and Dr. R. H. Seifert will continue as secretary-treasurer.

South Dakota

A NEW CLINIC has been established in Aberdeen by Drs. Alvin C. and Cleo L. Vogele. Located at 12th Ave. and Main St. S., the new facility will have a full complement of specialists and offer laboratory and X-ray services plus a pharmacy.

* * * *

DR. WILLIAM D. TRUMPE, a psychiatrist from Cedar Rapids, has joined the professional staff at Fort Meade Veterans Administration Hospital. A native of Evansville, Ind., Dr. Trumpe received his medical degree from the University of Illinois in Chicago in 1945, and interned at the university's Research and Educational Hospitals. He is a member of the American Psychiatric Association.

* * * *

DRS. ROBERT J. FOLEY and ALAN H. DOMINA of Tyndall have announced formation of a professional partnership. Dr. Domina, formerly a surgical resident at the Veterans Administration Hospital in Lincoln, Neb., has been associated with Dr. Foley in the Tyndall Clinic since this past summer. The two physicians also said that construction is progressing on the new medical center immediately west of St. Michael's Hospital and they plan to move in this spring.

* * * *

DR. JOHN T. ELSTON of Rapid City has been elected chairman of the Pennington County Board of Health. Dr. Elston was graduated in 1945 from the State University of Iowa College of Medicine and is a member of the College of American Pathologists and the American Society of Clinical Pathologists.

Deaths . . .

DR. RICHARD THOMAS MAXWELL, 54, Clear Lake surgeon and general practitioner, died of a heart attack Feb. 3. Prior to retirement last October he had been in practice in Clear Lake for 26 years. Dr. Maxwell was a 1935 graduate of the University of Colorado School of Medicine.

* * * *

DR. FREDERICK W. WITTICH, 80, retired St. Louis Park allergist, died Feb. 3. Born in Pennsylvania, he was a 1913 graduate of Johns Hopkins University School of Medicine. Dr. Wittich's interest in allergy began early in his career. He was the first to demonstrate atopy and was credited with being the first to liberate histamine from human blood. Founder and first president of the International Association of Allergology, he also was president emeritus and one of the chief founders of the American College of Allergists. Dr. Wittich was editor of the Review of Allergy and Applied Immunology and a former faculty member of the University of Minnesota.

* * * *

DR. OTTO WM. YOERG, 78, Minneapolis, died Jan. 27. A 1910 graduate of the University of Minnesota Medical School, Dr. Yoerg served on the staff of Northwestern Hospital for forty years before his retirement.

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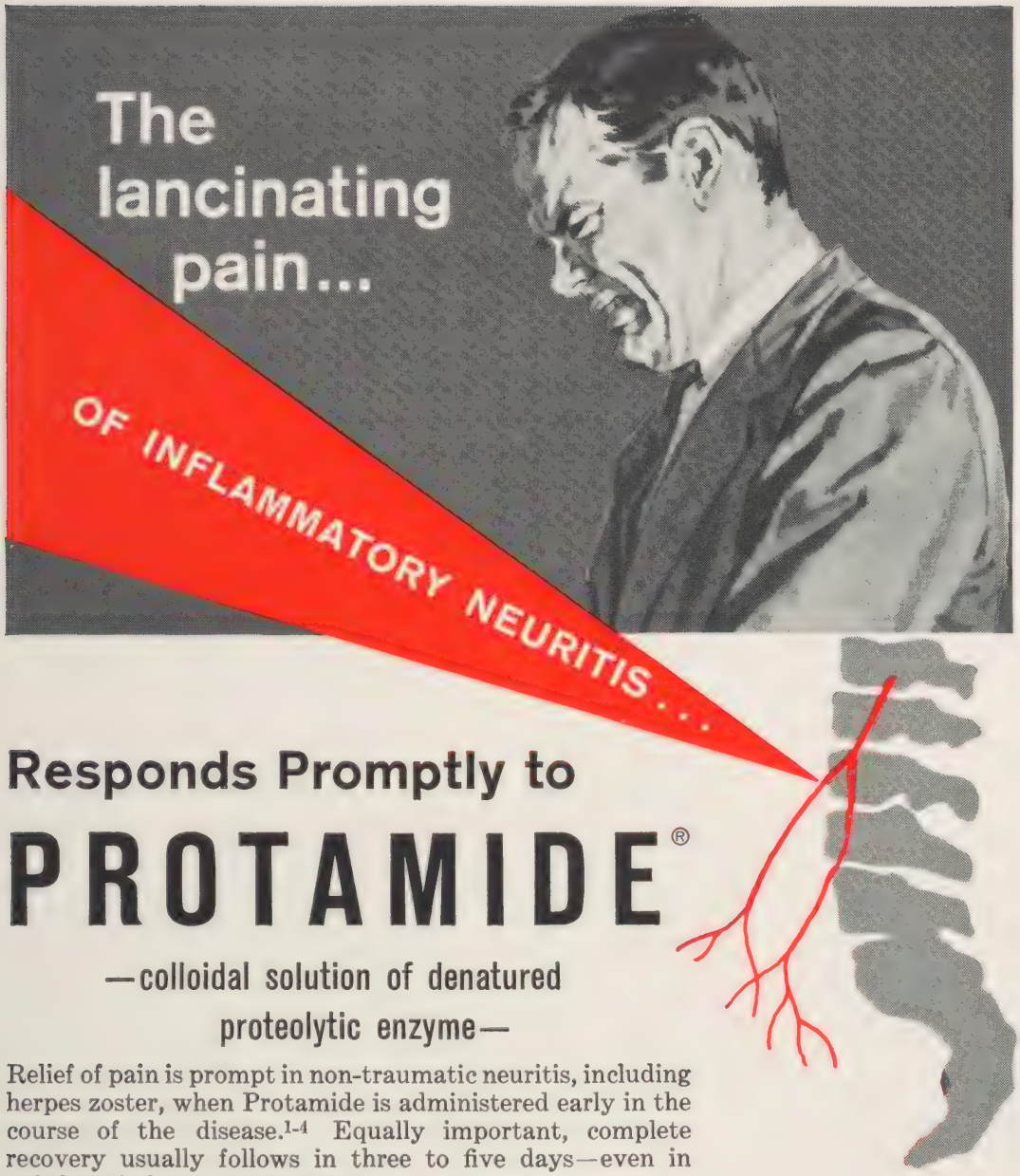
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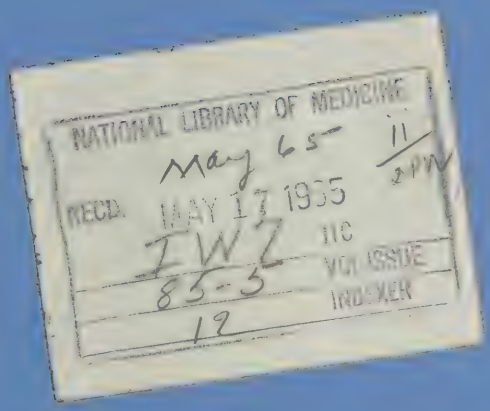
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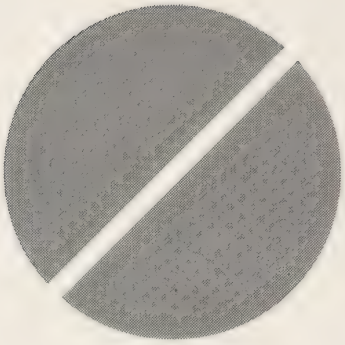
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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, 22:527, 1964.

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*Monti, A. A. F.: Rev. Bras. Cir. 43:288-297 (Apr.) 1962.

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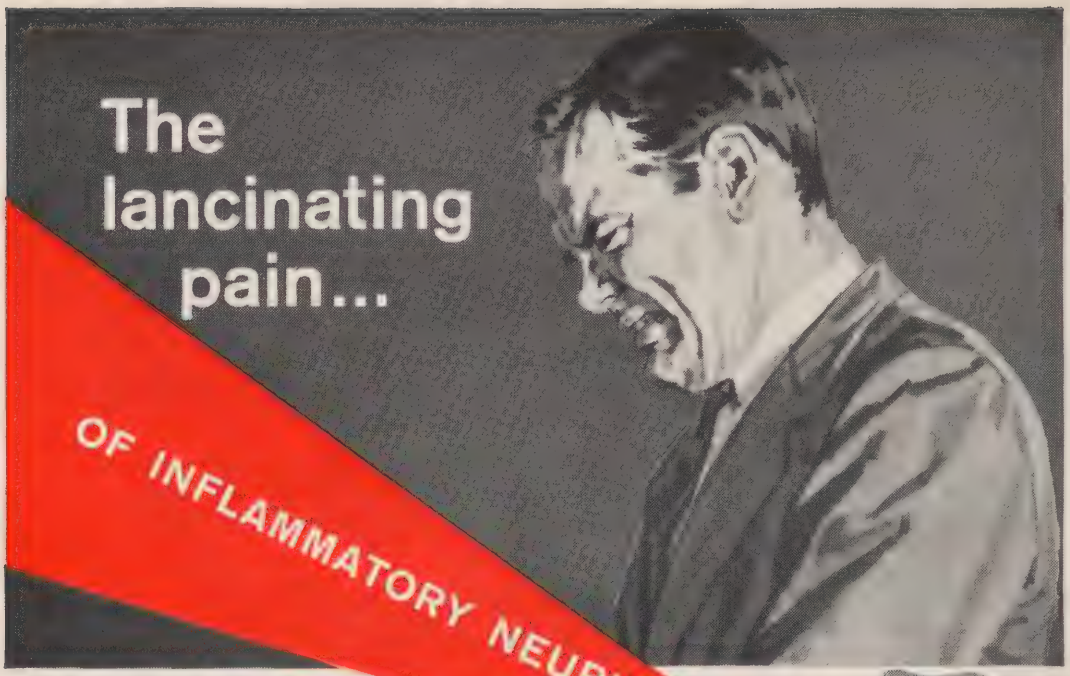
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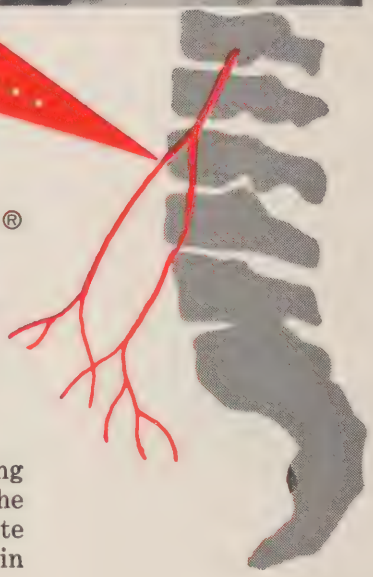


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References: 1. Baker, A. G.: Penn. Med. J. *63*:697 (May) 1960. 2. Smith, R. T.: New York Med. (Aug. 20) 1952, pp. 16-19. 3. Smith, R. T.: Med. Clin. N. Amer. (Mar.) 1957. 4. Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. (Nov.) 1955. 5. Sforzolini, G. S.: Arch. Ophthal. *62*:381 (Sept.) 1959. 6. Gile, J. H.: W. Virginia Med. J. *59*:120-122 (May) 1963.

The Journal-Lancet Volume 85, No. 5, MAY 1965

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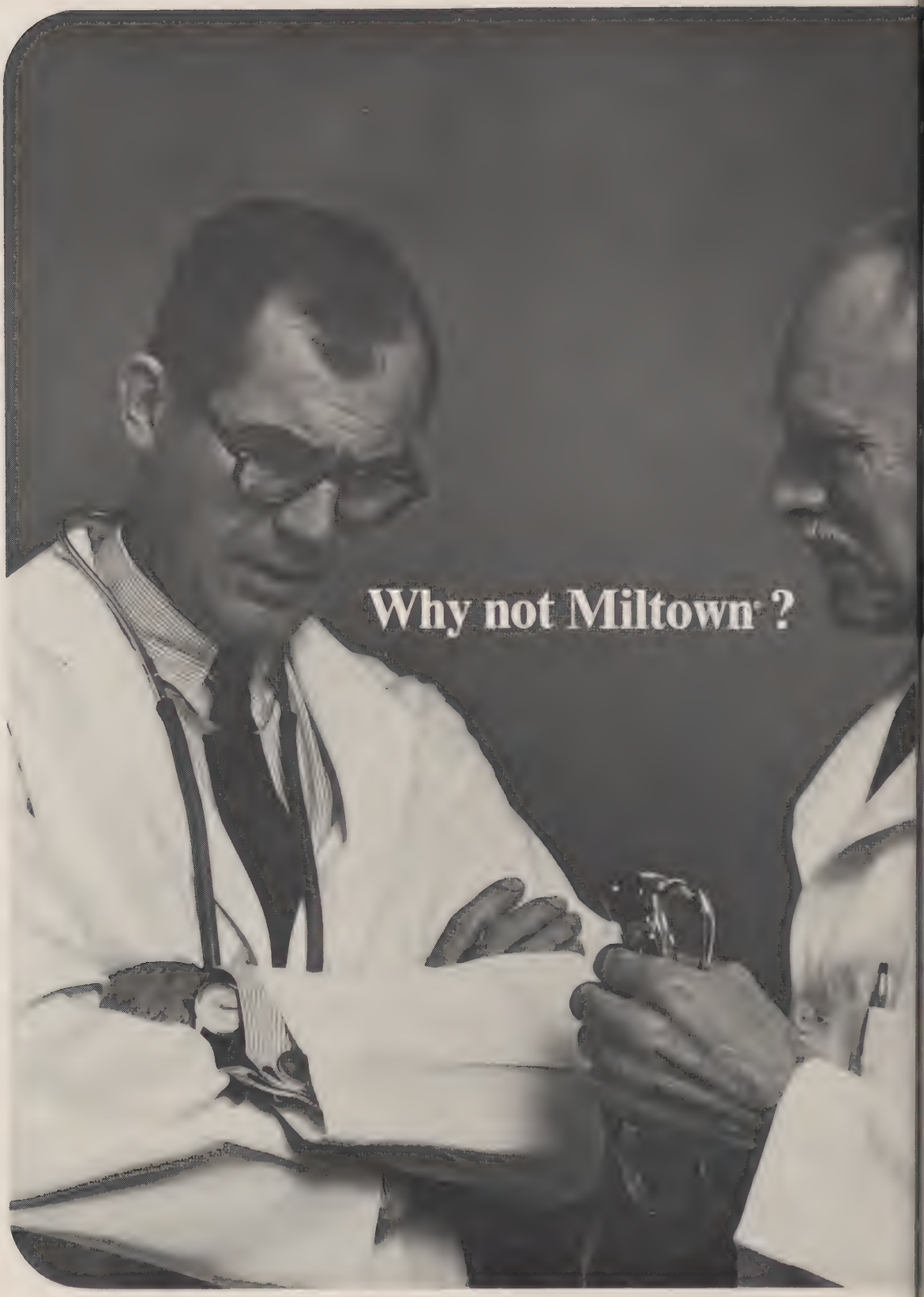
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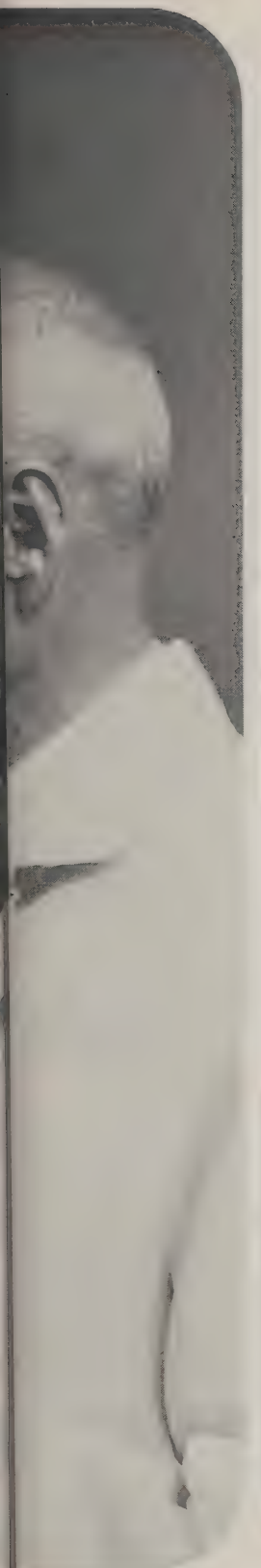
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1. Griffith, R.S., and Black, H.R.: Current Ther. Res., *6*: 253, 1964.

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THE JOURNAL-LANCET in June will be a special issue on pediatrics from the University of Marquette Medical School. Under the direction of Dr. J. C. Peterson, chairman of the department of pediatrics at Marquette, a splendid series of papers presenting an appropriate balance of clinical and basic research projects has been prepared. One of the papers will be illustrated in full color. The contributions include:

- **Forward,** by J. C. Peterson, M.D.
- **Copper Sulfate as an Emetic,** by Franklin Mellencamp, M.D.
- **Hemorrhage in the Newborn,** by Armand J. Quick, M.D.
- **Foreign Bodies in the Alimentary Tract of Infants and Children,** by John Erbes, M.D., and Donald P. Babbitt, M.D.
- **Thymic Alymphoplasia with Pancreatic Fibrosis and Mucoviscidosis,** by Efstathios Beltaos, M.D., and Samuel R. McCreadie, M.D.
- **Post Rubella Thrombocytopenia Purpura,** by Howard Lokietz, M.D., and Frank A. Reynolds, Captain U.S.A.F. (M.C.)
- **Hereditary Nephritis and Deafness,** by K. P. Nichol, M.D., and A. Miller, Ph.D.
- **Studies in Histidinemia,** by Stanley Berlow, M.D., Robert Arends, Ph.D., and Carol Harries, B.S.
- **Ritter's Disease,** by Archebald R. Pequet, M.D.

This special issue is the second of the series devoted to the field of pediatrics that has been planned by Dr. John A. Anderson, one of THE JOURNAL-LANCET editors and professor and head of the department of pediatrics, University of Minnesota. The series will be continued at intervals throughout 1965 and 1966. To appear subsequently are issues from the University of Oklahoma, the University of Arkansas, the University of Nebraska, and the University of Manitoba.



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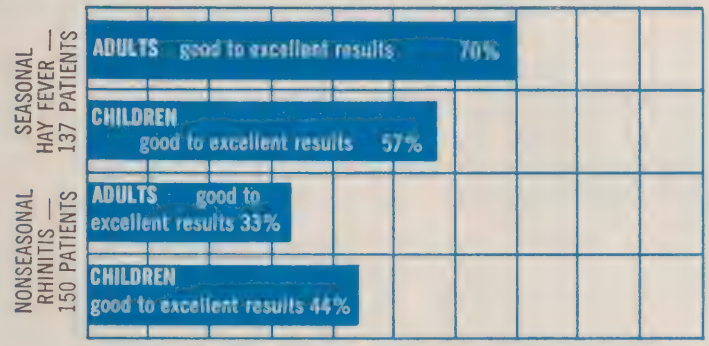
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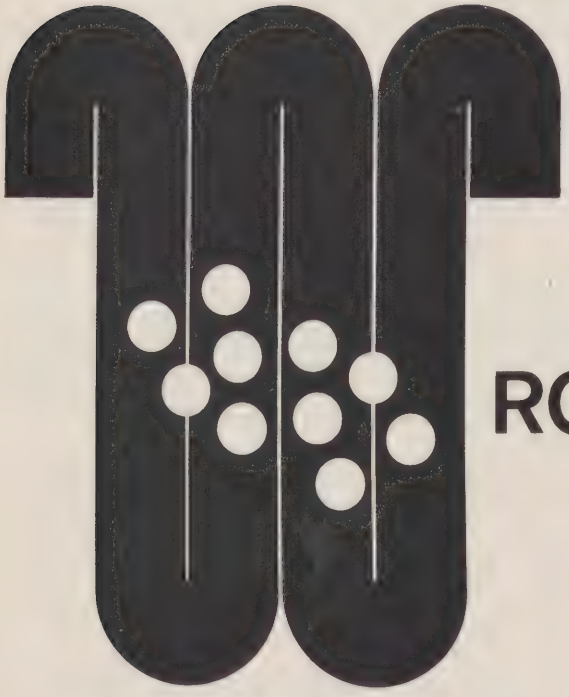
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Cardiac Emergencies

JAMES H. KELLY, M.D.

St. Cloud, Minnesota

Series on CARDIOVASCULAR DISEASE *for the* PRACTITIONER

The Executive Committee of the Minnesota Chapter of the American College of Chest Physicians accepted the invitation of THE JOURNAL-LANCET *editors to undertake a series of articles on cardiovascular disease. Dr. John F. Briggs was assigned the responsibility of developing the series.*

JAMES BELLOMO, M.D., President

THE ADVANCES in management of cardiovascular disease in the past few years are fantastic. Congenital heart disease is readily diagnosed and usually successfully treated. Rheumatic fever has been controlled, and luetic heart disease has almost vanished.

Subacute bacterial endocarditis is no longer the dread complication of valvular heart disease. The treatment of the arrhythmias as well as the surgical "cure" of complete heart block by pacemaker implant has favorably changed the prognosis in these conditions. Electrocardiography and radiology have entered a new era contributing to our knowledge and diagnostic ability.

Our knowledge and treatment of the degenerative diseases have bettered the prognosis for those people who suffer from these diseases. More and more people with heart disease are being returned to a normal socioeconomic and community life because of these advances. This paper by Dr. Kelly and those to follow reflect in a small way the progress made in cardiovascular disease.

JOHN F. BRIGGS, M.D.

AT THE PRESENT TIME more deaths occur in this country due to cardiovascular disease than from any other cause. Many of these deaths are the end result of chronic disease. Other deaths occur as a result of an abrupt change in the patient's cardiovascular status. Such emergent situations may be a complication of a known preexisting cardiac illness or may be the first symptoms of previously undetected cardiac disease. If appropriate therapy can be instituted promptly, many such situations are reversible. Although the management of cardiac emergencies has been adequately covered before,[1–3] it seems appropriate to periodically review the diagnosis and treatment of cardiac emergencies. One seldom can do so when confronted abruptly with the problem. No attempt will be made to cover each disease entity in detail. Emphasis will be placed on the immediate therapy of emergent situations as they arise in the cardiac patient.

CORONARY OCCLUSION RESULTING IN MYOCARDIAL INFARCTION

This is easily recognized when pain is typical. Usually the pain is substernal, radiating to one or both arms, neck, jaw, or back. Radiation to the left supramammary area is most common. The character of the pain varies widely but is most often described as "crushing" or "pressure." The pain usually waxes and wanes and is often ac-

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companied by sweating and dyspnea. The duration of the pain may vary from a few minutes to several hours, although most classic coronary pain, lasting more than thirty minutes, is due to myocardial infarction. Many patients with subsequently proven myocardial infarction experience little or no pain. "Stabbing" chest pain localized to the left lower anterior chest is almost invariably due to anxiety regarding heart disease and not due to myocardial infarction. Cardiac auscultation may reveal muffled or faint heart tones but is seldom diagnostic initially. In the presence of symptoms strongly suspected of myocardial infarction, the patient is best treated presumptively, as such, until such corroboratory studies as serial electrocardiograms, serum glutamic oxalacetic transaminase, erythrocyte sedimentation rate, and leukocyte counts can confirm or refute initial clinical impression.

Relief of pain and anxiety is paramount and in my experience is best accomplished by giving morphine sulfate, 15 mg. intramuscularly immediately. If the patient appears to be in shock, half of this may be given intravenously. Strict rest is important and if it is necessary to transport the patient, it should be done by ambulance or by whatever means are available that will require the least activity on the part of the patient. Adequate oxygenation is important and best obtained by nasal catheter or mask. If the pain persists, it may be necessary to repeat morphine at two-to-three-hour intervals. If severe pain is uncontrolled initially, it may be necessary to repeat morphine, 10 to 15 mg. in thirty minutes. Once the patient's initial symptoms are controlled and he has been transported to a cardiac treatment area, the less emergent therapy such as digitalis, quinidine, anticoagulants, laxatives, and so forth can be administered as needed.

The complications of myocardial infarctions such as cardiogenic shock, pulmonary edema, cardiac arrhythmias, embolization, and cardiac rupture will be dealt with as follows:

CARDIOGENIC SHOCK

This is most commonly encountered following severe myocardial infarction and is a very poor prognostic sign. In the milder forms, treatment with metaraminol (Aramine®), 10 mg. intravenously or intramuscularly will suffice, but if this fails, l-noradrenaline (Levophed®) intravenously should be used. Levophed®, however, has the disadvantage that it must be used intravenously, adding additional fluid to an already compromised circulation. Vasopressors should be used to a degree necessary to maintain adequate blood flow to vital organs but not necessarily to restore normal blood pressure. Clearing of mental confusion, diminution in cardiac pain, and maintenance of adequate urine output are easily observed clinical indications of improved perfusion of brain, heart, and kidneys. Phenoxybenzamine (Dibenzyline®) and massive doses of hydrocortisone are currently under clinical investigation in the treatment of cardiogenic shock. These methods of treatment look very promising.

ACUTE PULMONARY EDEMA

This is most often associated with severe forms of hypertensive cardiovascular disease or aortic valve disease. It may be the only initial manifestation of an acute myocardial infarction and, on occasion, is iatrogenically produced by the overzealous administration of intravenous saline, especially in the early postoperative period. Acute pulmonary edema may also occur in ischemic heart disease without infarction, other valvular heart disease, endocrinopathics, inflammatory processes, and deficiency syndromes. This is not a complete etiologic list but indicates the importance of making an emergency diagnosis if possible, adjusting therapy as indicated. When due to left ventricular failure, it may have been preceded for some time by episodes of paroxysmal nocturnal dyspnea. The patient presents as a dyspneic, anxious person who is orthopneic. Very early in paroxysmal pulmonary edema the lungs may be clear, but within a few minutes moist rales appear throughout the chest, especially prominent at the lung bases. Wheezing due to bronchiolar spasm is often heard. This, on occasion, causes a mistaken diagnosis of bronchial asthma to be made. Treatment consists of prompt administration of morphine, 15 mg., or meperidine (Demerol®), 100 mg. intravenously, aminophylline, 500 mg. intravenously slowly, lanatoside c (Cedilanid®), 0.8 mg. intravenously initially, and 0.4 mg. every two hours for a total dose of 1.6 to 2.0 mg., depending on the patient's size and therapeutic response. A mercurial diuretic such as mercaptomerin sodium (Thiomerin®) and oxygen by nasal catheter or mask, and in severe cases positive pressure apparatus, can be administered. Applying tourniquets to the 3 extremities not being used for medication administration, at a pressure to occlude venous return but not arterial flow, is helpful but must be released in rotating fashion every ten minutes so that no limb is occluded excessively. It is often easier and more effective to do a phlebotomy of 500 to 1,000 cc. The emergency treatment of pulmonary edema must necessarily be individualized. The importance of a confident, reassuring

manner on the part of the physician and other personnel, while administering therapy promptly, should be emphasized.

THE ARRHYTHMIAS

Paroxysmal tachycardias are the most common arrhythmias giving rise to cardiac emergencies. Some may occur in people with normal hearts, whereas more commonly they are present in patients with preexisting heart disease. In the latter, these arrhythmias may constitute life-threatening complications, whereas a normal heart can withstand rates up to 180 per minute for twenty-four to forty-eight hours without serious consequence. In any case, these occurrences are always a cause of anxiety to the person experiencing them. Characteristically, paroxysmal tachycardias begin and end abruptly. It is most important to accurately diagnose paroxysmal arrhythmias because in the supraventricular variety, that is, paroxysmal atrial tachycardia, nodal tachycardia, atrial flutter, and atrial fibrillation, digitalis may be the initial therapy of choice. In ventricular tachycardia or fibrillation the initial drug of choice is quinidine or procaineamide (Pronestyl®). Many supraventricular paroxysmal tachycardias respond simply to rest and sedation or both, but their occurrence in the presence of known organic heart disease, such as mitral stenosis or following myocardial infarction, usually requires more aggressive therapy. Symptoms related to the supraventricular tachycardias vary from no symptoms to extreme prostration.

Atrial and nodal tachycardia commonly occur in young people with no underlying heart disease. It also occurs commonly in patients with organic heart disease. One suspects this, clinically, because of its abrupt onset and ending, absolutely regular rhythm at a rate greater than 160 per minute. If possible, clinical impressions should be confirmed electrocardiographically. Treatment consists of various maneuvers such as prolonged breath holding, induced vomiting, or carotid sinus massage. If these maneuvers are unsuccessful, sedation with Demerol®, 100 mg. intramuscularly, or morphine, 10 to 15 mg. intramuscularly, may be used. If the tachycardia persists and if the patient has not been receiving digitalis, Cedilanid®, 0.8 to 1.6 mg. intravenously, will often terminate the tachycardia. Often vagal stimulation plus digitalis is necessary. Quinidine therapy following Cedilanid® will sometimes be required to terminate the attack. Reserpine, 0.25 mg. orally 2 to 3 times daily, is often good adjunctive therapy.

In atrial fibrillation the apical cardiac rate is rapid and grossly irregular. Digitalization to slow the rate to 70 to 80 per minute is advisable and on occasions converts rhythm to a sinus rhythm. Quinidine therapy following digitalization will often convert fibrillation to sinus rhythm. Those not converting on digitalis-quinidine therapy should be considered for electrical cardioversion.[4,5]

Atrial flutter is usually paroxysmal but may be persistent in which case it may be quite refractory to medical treatment. The rate is regular, usually 140 to 180 per minute, but varies with the degree of atrioventricular block. One can often observe and count the rapid atrial contractions in the neck veins. Carotid sinus stimulation may increase the degree of atrioventricular block causing a transient, abrupt drop in ventricular rate, usually half the initial rate. The treatment, medically, is full digitalization. If this is not successful, cardioversion should be considered because of the highly successful results with this method.[4,5]

Atrial tachycardia with block is usually present in patients with organic heart disease on digitalis therapy. The rate is variable depending on the degree of block. Treatment involves withholding digitalis and giving potassium chloride, 1 to 2 gm. orally every four hours, or 40 mEq. of potassium chloride intravenously in 5% glucose in distilled water. Diphenylhydantoin (Dilantin®) has also been found to be beneficial in treating such digitalis-induced arrhythmia. Two hundred fifty to 500 mg. intravenously or intramuscularly, in divided doses, depending on the patient's size and response, is the usual dosage. If not due to digitalis toxicity, the arrhythmia is treated as atrial flutter.

Ventricular tachycardia is usually due to organic heart disease, most commonly coronary artery disease. It may also be caused by excessive doses of digitalis, quinidine, or vasopressors. The rate is usually 150 to 250 per minute. It varies slightly as compared to supraventricular tachycardia which does not vary at all. Vagal stimulation by carotid sinus massage has no effect. Electrocardiographic confirmation is important. Treatment, if the situation is not critical, involves giving Pronestyl®, 1,000 mg., every four hours orally for a total of 5 doses, or until an effect is obtained. In more critical patients, which is usually the case, give Pronestyl®, 100 mg. intravenously every five minutes to a total maximum dose of 1 gm. Electrocardiographic monitoring and constant observation for hypotension are important. Hypotension should be managed with vasopressors such as Aramine®, 5 to 10 mg. intravenously. Marked widening of QRS complex

or worsening of cardiac rhythm are indications to stop Pronestyl® injection. Usually 250 to 500 mg. of Pronestyl® will terminate an attack. As much as 4 gm. of Pronestyl® has been used in special circumstances to successfully control ventricular tachycardia, resistant to more conventional therapy.[6]

Ventricular fibrillation and ventricular standstill are most often the terminal event in chronic progressive heart disease. However, this may occur abruptly in patients with relatively healthy hearts otherwise capable of efficient function, for example, in electrical shock, asphyxia, or anesthesia or following acute myocardial infarction. Recent introduction of closed chest cardiac massage by Kouwenhoven and Jude has permitted the salvage of many lives without resort to thoracotomy with its greater technical difficulties and risks. If a patient is to be saved from this type of catastrophe, prompt institution of adequate oxygenation by artificial respiration (mouth to mouth) and external cardiac massage to maintain circulation artificially must be accomplished by personnel in attendance at the time. Emergency cardiac arrest equipment and personnel must be quickly obtained or the patient must be transferred promptly to an adequately equipped emergency area. A diagnosis as to the exact type of cardiac catastrophe can then be made and more definite treatment applied. This may include use of electroshock using the external defibrillator in ventricular fibrillation or the external cardiac pacemaker in cardiac standstill.

Detailed discussion of this topic is beyond the scope of this paper. A point worthy of emphasis is that all patients with ventricular fibrillation or standstill need not die. However, successful treatment depends on prior training of all personnel likely to encounter cardiac arrest, in the proper immediate application of external cardiac massage, and in a previously planned and rehearsed cardiac resuscitation program in every hospital. Such a program must be a team effort involving nurses, physicians, anesthetists, and technicians. Examples of this type of cooperative effort have been previously published.[7–16]

COMPLETE HEART BLOCK

The clinical course of complete heart block is quite variable. It may become evident as severe circulatory embarrassment at the onset or it may be present for many years without symptoms. It is usually seen in the presence of long standing arteriosclerotic heart disease. The ventricular rhythm is slow and regular, and varying intensity of the first heart sound may be noted on auscultation. Asystole—ventricular standstill—may occur at any time resulting in syncope, convulsions, or death due to Adams-Stokes syndrome, depending on the length of asystole. Ideally, reestablishment of normal atrioventricular conduction is the best method of treating atrioventricular block. In acute heart block the use of atropine to abolish vagal depression of the atrioventricular node, aminophylline to improve nodal circulation, and adrenal steroids to reduce any inflammatory process about the atrioventricular node may be beneficial. Unfortunately, complete heart block often presents as a severe Adams-Stokes syndrome and cannot be treated ideally. In the acute situation, intravenous injection of epinephrine of 0.5 cc. of 1:1000 solution, or isoproterenol (Isuprel®), 0.2 mg., or an acute blow on the chest may revive ventricular contraction. If neither is successful, intracardiac injection of epinephrine or Isuprel® may produce mechanical, followed by pharmacological, stimulation of the ventricles. The patient is then attached to an electrocardiographic monitor and external electrical pacemakers and an intravenous infusion of Isuprel® is started promptly, using a concentration of 2 mg. per 1,000 cc. of 5% glucose in distilled water, at a rate of 2 cc. per minute. An effort is made to maintain an idioventricular rhythm of 40 to 50 per minute which occasionally requires concentrations of Isuprel® as high as 10 mg. per 1,000 cc. of solution. The use of Pronestyl® or quinidine is contraindicated in the presence of atrioventricular dissociation. Recent improvement in electronics and surgical techniques has made implantation of artificial cardiac pacemakers the treatment of choice in many patients with recurrent attacks of asystole due to complete heart block.[17]

PULMONARY EMBOLI

These usually result from venous thrombi in the pelvic veins or deep leg veins, often in postoperative patients or in patients restricted to bedrest for prolonged periods. Trauma may also be a factor in initiating such thrombi. Emboli may also arise from the right atrium in patients with atrial fibrillation. There is no classical, clinical picture in pulmonary embolism. However, pleuritic type pain, dyspnea, tachycardia, and apprehension are suggestive. The time-honored diagnostic symptoms of cough and hemoptysis are commonly absent. This is especially true in a massive embolus or in chronic, repeated, small emboli. The pain may be indistinguishable from that of myocardial infarction but fortunately the emergency therapy of the 2 conditions is essentially the same.

CARDIAC TAMPONADE

This may be due to pericarditis or trauma. It may also be secondary to cardiac rupture or dissection of the base of the aorta. Clinical symptoms and physical findings are those of marked increase in venous pressure with paradoxical pulse, increasing dyspnea, increased cardiac dullness, and diminished heart sounds. The increased venous pressure is easily measured and is extremely high. The carbon dioxide cardiogram, a radiologic technique now generally available, will often differentiate pericardial effusion from cardiomegaly without effusion. Pericardiocentesis is both diagnostic and therapeutic. Following emergent removal of fluid due to inflammatory processes, more definite diagnostic studies are in order. The advent of more sophisticated cardiac surgery makes diagnosis of cardiac rupture more than academic and on a rare occasion a life may be saved by prompt recognition.

DISSECTING ANEURYSM OF THE AORTA

Recognition of this uncommon condition is important for 3 reasons: (1) It frequently resembles myocardial infarction, (2) surgery therapy may be feasible, and (3) anticoagulants are often best avoided. It most often occurs in elderly hypertensive males but may occur during pregnancy or as a complication of coarctation of the aorta or Marfan's syndrome. The pain is usually knife-like, starting in the chest and radiating to the back, head, neck, and shoulders and often to the abdomen and legs. The pain is rapid in onset, beginning with its maximum intensity which is unlike myocardial infarction pain which increases gradually in intensity. Syncope and shock may quickly supervene, but curiously, even in presence of obvious clinical shock, the blood pressure may remain normal for a period of time before falling abruptly. Disappearance of any peripheral pulses should be looked for. Anuria may be present. The electrocardiogram is usually normal or shows nonspecific abnormalities. The chest X-ray may show widening of the aorta, often with a double shadow. Evidence of pleural or pericardial effusion may be present. Treatment involves strict rest and morphine, 15 mg., or Demerol®, 100 mg., repeated as necessary to insure rest. In the presence of hypotension, vasopressors should be used cautiously to keep a systolic pressure of 90 to 100 millimeters of mercury, being careful not to push the systolic pressure higher. The use of corticosteroids such as intravenous hydrocortisone, 100 mg., may enable use of lesser amounts of vasopressors. If the condition is recognized clinically and the patient survives the initial insult, subsequent arteriography and vascular surgery may be lifesaving.

IATROGENIC CAUSES AND CONTRIBUTORS TO CARDIAC EMERGENCIES

Digitalis may result in nausea, anorexia, diarrhea, melancholia, headache, irritability, and even delirium and ataxia. Bizarre visual complaints are quite common and, on occasion, pain in the lower part of the face is noted. Arrhythmias may occur with or without the above subjective symptoms. Ventricular ectopic beats are most common. Nodal tachycardia is also seen as a complication of digitalis therapy. An important arrhythmia is atrial tachycardia with block since further digitalis therapy in such a case may be fatal. Since the advent of the thiazide drugs with their potent kaliuretic effect, digitalis intoxication has been seen much more commonly. Usually withdrawal of digitalis and administration of potassium is adequate treatment. Recently, citrate and Dilantin® have been used very effectively.

Quinidine may result in diarrhea, tinnitus, nausea, blurred vision, or purpura. Aberrant rhythms may develop and are especially ominous if the QRS complexes have become widened. There is also the risk of hypotension. Pronestyl® may cause similar side effects but they are generally less frequent and less severe. Acute pulmonary edema is seen more often in patients receiving medications such as the various steroids which enhance sodium retention. My most recent experience of this sort was in an elderly man with arteriosclerotic heart disease receiving stilbestrol for carcinoma of the prostate.

SUMMARY

An effort has been made to briefly review existing information on the diagnosis and treatment of those conditions most likely to give rise to cardiac emergencies. Emphasis has been placed on information the clinician should possess to promptly suspect the correct diagnosis and institute appropriate therapy.

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Evaluation of the Duhamel Type Operation for Hirschsprung's Disease

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THE SURGICAL MANAGEMENT of aganglionic megacolon continues to pose many problems. No truly suitable surgical therapy existed until the work of Swenson and Bill[1] in the period, 1946 to 1948. Since that time, the Swenson pull-through has been more or less accepted as the procedure of choice. Because it is a difficult and time-consuming operation, fraught with dangers and complications even in experienced hands, it is not surprising that many variations and alternative treatments have been devised and advocated. Undoubtedly, many more procedures are yet to be conceived and will be advocated with equal enthusiasm.

At the present time, we are trying to evaluate the operation, or a modification of the operation, devised by Dr. Bernard Duhamel[2] in 1956. Our operation is completely illustrated and discussed elsewhere.[3] Although our series is small, certain conclusions can be drawn from a review of our problems and those of others testing the procedure.

Certain complications and undesirable effects may accompany any operative procedure, whether it be of the Swenson or Duhamel type. In this respect, it is my clinical impression that the duration and extent of any operative procedure seem to bear a direct relationship to the incidence of postoperative complications.

The proponents of the Duhamel operation point out several advantages over other operations:

(1) It requires very little pelvic dissection and, thus, should not endanger the genitourinary system in any way and should minimize risk to the pelvic nerve plexuses. (2) It is a relatively simple and less time-consuming operation. (3) Because of points 1 and 2, there is very little loss of blood. (4) Because of points 1, 2, and 3, it can be performed on even a tiny infant. (5) The resultant anastomosis theoretically produces a functioning rectum in which the sensory pathways are left intact and a "gusset" of ganglionic bowel is inserted in the posterior wall of the aganglionic rectum to provide normal sensation. (6) The nature of the procedure permits a satisfactory anastomosis of two limbs of bowel even when a marked disparity in size exists.

Specific objections to the Duhamel operation, both in theory and in practice, have included: (1) The blind rectal pouch may become the site of fecal impaction. (2) The stoma created with clamps may tend to stenose or may be too small when healing is complete. (3) Soiling or some degree of incontinence may result. (4) The clamps may fail to approximate the limbs of bowel adequately and so produce leakage.

Except in patients with aganglionosis up into the small bowel, I attempt to make the blind rectal pouch as short as is conveniently possible. I now use long, heavy 8-in. Ochsner-Dixon clamps, one curved and one straight, in order to carry the final stoma as near to the apex of the pouch as possible. In this way, I hope I am eliminating objections 1 and 2 and possibly 4.

Any comparison of 2 procedures is difficult and, in most instances, unfair to one or the other operation on almost every count. Having a fairly large personal series of patients treated basically by the Swenson type pull-through operation, it is now my desire to evaluate the Duhamel type procedure with which I have had considerably less experience.

The initial attractive advantage of the Duhamel operation is its lack of pelvic dissection.

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Superimposed mattresses provide a shelf over which the clamps may project.

Certainly, it is reassuring to the surgeon and, eventually, to the male patient to know that no possible injury has befallen the reproductive mechanism. I first became interested in the operation when I had to treat an infant with a proved diagnosis of aganglionosis to the midileum. The thought that a very long gusset or even a series of anastomoses of the upper part of the ileum to the rectum and rectosigmoid could be established in the event that uncontrollable diarrhea persisted was comforting and inviting. In the 2 patients with aganglionosis to the midileum in our series of Duhamel operations, diarrhea has not been a problem.

The fact that the procedure is feasible on tiny infants in the first few weeks of life has been demonstrated by many surgeons. We have not yet seen fit to employ this on anyone under 1 year of age, but, undoubtedly, further experience and necessity will lead to its use in smaller infants.

While operating time should never become so important as to affect the technical quality, particularly in elective planned surgery, it is always desirable to employ the shortest procedure which will give the desired result. The Duhamel operation is certainly a much shorter procedure than the Swenson pull-through in my hands.

The presence of clamps protruding from the anus for five to seven days after operation is a real as well as a theoretical objection. The patients, however, have shown surprisingly little resistance or discomfort. I have felt compelled to restrain the smaller children during the period of use of clamps, but this type of protection is apparently not deemed necessary by most surgeons doing the operation. Skin traction and suspension of the clamps on an elastic band have been most satisfactory. Superimposed mattresses provide a shelf over which the clamps may project. Because of these anal clamps, greater attention to nursing care is necessary, but it is difficult to list this as a real disadvantage since this type of surgery should not be attempted without adequate nursing personnel.

It is impossible to evaluate the mortality rate in a small series of 14 patients with no deaths. Any procedure which is not performed with meticulous attention to hemostasis, accurate approximation of tissues, and good general surgical technique can produce hematomas, abscesses, fistulas, and adhesions. These situations must be recognized and treated accordingly or death may result. It is curious that our 2 youngest patients had postoperative adhesions that produced evidence of mechanical obstruction. Division of these adhesions has given complete relief.

There has been only very modest evidence of morbidity so far as fever, adynamic ileus, and

TABLE

DUHAMEL TYPE OPERATION FOR AGANGLIONIC MEGACOLON

Case	*Complications*
1	Pleural effusion (due to passage of cutdown catheter up and through the wall of the basilic vein)
2	*First operation:* Specially designed clamps without handles and teeth failed to hold and proximal bowel retracted with resulting fistula formation *Second operation:* Colostomy, abdominal drainage, and revision of anastomosis *Third operation:* Revision of anastomosis and excision of fistula *Fourth operation:* Closure of colostomy
3	5 stools daily (almost total colectomy), now reduced to 1 to 2 daily
4	Postoperative adhesions in epigastrium required laparotomy and lysing of adhesive band (9 months later, elsewhere)
5	5 to 6 stools daily at dismissal (ileoproctostomy), now reduced to 1 to 3 formed stools daily; stress ulcer (?) and anal fissure (fifth postoperative day)
6	None
7	None
8	Rectal bleeding and wound bleeding on eighth day postoperative; bleeding tendency at previous surgery (elsewhere); undiagnosed hematologic problem
9	None
10	Leak at anastomosis, temporary colostomy; patient had daily rectal examinations with clamps in place due to misunderstanding in management
11	None
12	Postoperative adhesive band required division (3 months postoperative, elsewhere)
13	Stenosis of stoma requiring reapplication of clamps
14	None

general discomfort are concerned. This is truly surprising in view of the complications which we have experienced in our series (Table).

It is rather early to assess the final results in these 14 patients since the first patient was operated on in May 1962. However, it is sufficient to state that the results seem to be highly satisfactory, with no evidence of any enterocolitis. Several of the patients are not yet old enough to be completely toilet trained. None has any detectable urinary problem and only in patient No. 2 has there been any soiling. This soiling has not been the type one would expect with surgical damage. The mother states that there is no soiling if the patient wants to be clean and that the rare episode is apparently an intentional controllable matter.

SUMMARY

The Duhamel operation appears to be relatively simple to perform, requires little dissection in the pelvis, and is a short operation. The morbidity is minimal, and the final results are satisfactory. Our complications have been numerous and varied. The complications in two patients (No. 2 and No. 13) could be attributed to the procedure but, in each case, our own deficiencies seemed responsible rather than the operation itself. Further experience is necessary before any final conclusions are justified; however, the results are sufficiently encouraging to warrant a more liberal use of the procedure, particularly in a younger age group. It is also possible that this will become the operation of choice for relief of symptoms resulting from inadequate initial surgical treatment for anganglionic megacolon.

Presented at the Fall Clinical Conference sponsored by the Quain and Ramstad Clinic and the Bismarck Medical Foundation, Bismarck, North Dakota, November 7, 1964.

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CARDIAC EMERGENCIES—

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The Psychiatry of Presidential Assassination

Part III: The Roosevelts

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PRESIDENT THEODORE ROOSEVELT AND JOHN N. SCHRANK, OCTOBER 14, 1912

The date was September 15, 1901; the time, 1:30 A.M., not quite twenty-four hours after President McKinley's death by an assassin's bullet. In a dream, John N. Schrank, a short, pudgy-faced, colorless immigrant, "saw [he later wrote] president McKinley sit up in his coffin, pointing at a man in a monk's attire. . . ." The monk was Theodore Roosevelt, and, Schrank wrote, "The dead president said This is my murderer, avenge my death."[10]

At the same hour on September 14, 1912, the eleventh anniversary of McKinley's death, Schrank, now 36 years old, was alone in his room, writing a poem. He felt a tap on his shoulder and heard a voice say: "Let not a murderer take the Presidential chair. Avenge my death." In a letter "to the people of the United States" written the next day, he avowed: "I could clearly see Mr. McKinley's features."[10] Within a week the auditory and visual hallucinations had overwhelmed his ability to deal with reality. He bought a .38-caliber Colt revolver and a box of cartridges and began to pursue the campaigning Roosevelt across country.

After the death of McKinley, Theodore Roosevelt had served the unexpired three and one-half years of that term and then had been elected to a four-year term. He was succeeded by William H. Taft (1909-13). In 1912 Roosevelt ran for President again, this time on the Progressive ticket. By so doing he collided with Schrank's strongest delusional conviction: that the greatest disaster that could happen to the country would be the violation of the two-term tradition for the Presidency. (Technically, Roosevelt had not served two terms.) With the announcement of Roosevelt's candidacy that August, Schrank's dream of eleven years before began to take on meaning for him. To become President, Roosevelt had provoked Czolgosz to kill McKinley, the dream seemed to tell him. Thus, to Schrank, Roosevelt had two unforgivable strikes against him: he was responsible for McKinley's assassination and he was flouting the two-term tradition.

John Schrank was born in Bavaria in 1876. Deprivation marked his childhood. His father died of tuberculosis at age 38. His mother, a cleaning woman, soon remarried and moved away, abandoning the boy to an uncle and aunt, Dominick and Anna Flammang. The Flammangs emigrated to New York City when John was 13. John eventually became a naturalized citizen.

As a young man, Schrank was gentle, orderly, and polite. All his emotional ties seemed to be to the Flammangs. A note found in his suitcase after the assassination said: "I never had a friend in my life. My uncle was more than a friend, and God has been my guardian." He did, for a while, have a girl friend, Emily Ziegler, but the relationship probably was not very close. It ended suddenly on June 15, 1904, when the steamship *General Slocum* burned in the East River. Emily was one of the more than 1,000 persons who lost their lives that day. Had Schrank been able to get someone to tend bar for him, he too would have been on the boat.

That year, Flammang retired, turning the saloon over to Schrank, now 28. He sold it two years later, perhaps because he was becoming too mentally ill to shoulder the responsibility. Reading and writing and wandering around New York City lost in dreams became his main activities. Anna died in 1910; Dominick, a year later. Schrank inherited a tenement worth about $25,000. He sometimes worked as a bartender. Essentially, however, he was preoccupied with schizophrenic fantasies and delusions.

In January of 1912 Schrank moved into a cheap room near the Bowery, doing little but reflecting on politics. Stimulated by his reading and thinking, he formulated four "unwritten

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laws," which he called "The Four Pillars of Our Republic." The two-term rule was one; the others were that the Monroe Doctrine should be supported, that the Presidency should be limited to Protestants, and that wars of conquest should be prohibited. His delusion about a third term may have been patterned after attacks newspapers were making on Roosevelt's candidacy.

Schrank prayed that God would find a leader among men to take the responsibility of killing Roosevelt. None appeared, and since he was a single man with no family ties, he decided the mission was his. He was aware that this decision might cost him his life, but he concluded that the cause warranted the sacrifice. Then came the vision in which the dead McKinley tapped him on the shoulder, and the die was cast. "When asked [at a pre-trial examination] whether he considered [McKinley's appearance] as imagination or as inspiration and a command from God, while showing some reluctance to claim the vision as an inspiration, he finally answered decisively that he did."[10]

Then began a long tour through the South and the Midwest, Schrank and his Colt revolver trailing Roosevelt from city to city. In Chicago on October 12 he passed up an opportunity to shoot Roosevelt because he did not want to damage the reputation of that city. The candidate was to speak next in Milwaukee. Schrank arrived there on October 13, rented a room, and waited until the following evening, when Roosevelt was scheduled to speak. Soon after his arrival at 5 P.M. Roosevelt was persuaded to attend an informal dinner at the Hotel Gilpatrick; his presence there quickly became known. In the crowd waiting outside to see the former President was Schrank, his revolver tucked in his trousers. Night had fallen when Roosevelt walked from the hotel and entered his open car, which had been waiting at the entrance to take him to the city auditorium for his speech. As the candidate stood in the back seat to wave to the crowd, Schrank, only 6 ft. away, shot between the heads of the men in front of him. Roosevelt fell back, the bullet having struck him in the right breast. With amazing presence of mind, he coughed into his hand. Seeing no blood, he knew that the slug had not penetrated his lung and that the wound, although bleeding profusely, was probably not lethal. As it turned out, and Roosevelt later credited this circumstance with saving his life, the bullet had traveled through his metal spectacle case and 100 pieces of paper (a 50-page speech folded double), which he was carrying in the breast pocket of his coat. The rest of its force had been spent in fracturing a rib.

Immediately after the shot, Roosevelt's secretary, Elbert Martin, a former college football player, knocked Schrank down with a flying tackle before he could fire again. Some of the crowd wanted to lynch Schrank, but Roosevelt intervened; the gunman was taken into the hotel and, by back door, to police headquarters.

In the best tradition of the stage, Roosevelt directed that he be driven to the lecture hall. He delivered his 50-page speech, apparently filling in around the two bullet holes on each page, while the red spot on his shirt widened. A crowd of 9,000 alternately cheered him and begged him to go to the hospital. After the speech, which lasted fifty minutes, he was taken to an emergency hospital. Soon after midnight he was transferred to a Chicago hospital, where he quickly recovered. The public, although impressed with Roosevelt's courage, elected Woodrow Wilson.

To his examiners after his arrest Schrank was open and helpful. "He gave as a reason for his attack upon Roosevelt, that he did not wish to give him (Roosevelt) an opportunity to plead that no defense of the Third Term tradition had been made in 1912 should he aspire to another term in 1916. Asked as to how he reconciled his act with the commandment 'Thou shalt not kill,' he replied that, 'religion is the fundamental law of human order, but to kill to try and do a good thing, and to avenge McKinley's murder, justifies the killing.' "[10]

In Schrank's pocket after his arrest was the letter to the American people in which he told of his dream of 1901 and his vision of 1912. "Before the Allmightly god, I swear that the above written is nothing but the truth," he wrote below his description of the phenomena. Among his personal papers was a bill on which he had written, "Theodore Roosevelt is in conspiracy with European monarchs to overthrow our Republic. Theodore Roosevelt's unscrupulous ambition has been the murder of President McKinley to satiate his thirst for power. Down with Theodore Roosevelt. We want no King. We want no murderer. The United States is no Carthage. We will not yield to Rome."[1]

On November 13 the Municipal Court of Milwaukee appointed a sanity commission of 5 psychiatrists. Ten days later they submitted a report in which they unanimously concluded that Schrank was psychotic, that he was "suffering from insane delusions, grandiose in character, and of the systematized variety."[11] After the physicians testified separately that the prisoner was mentally ill, the trial was stopped.

Schrank spent the rest of his life in Wisconsin mental hospitals, dying of arteriosclerosis and

pneumonia at age 67 on September 15, 1943. He apparently held no animosity toward Theodore Roosevelt, calling him a great American at the time of his death in 1919. But Schrank became disturbed in 1940 when Franklin D. Roosevelt ran for a third term and stated that if he were free he would try once again to save the nation.

Schrank, like assassins before him, had considered himself to be an agent of God and had been sure that he would be recorded in history as a hero. His illness can be diagnosed as paranoid schizophrenia.

FRANKLIN DELANO ROOSEVELT AND GIUSEPPE "JOE" ZANGARA, FEBRUARY 15, 1933

Like his fifth cousin twenty-one years before, Franklin D. Roosevelt was the subject of an assassin's plans. Theodore was wounded by John Schrank; Giuseppe Zangara missed Franklin D., but one of his bullets killed Mayor Anton Cermak of Chicago. Although undoubtedly psychotic, Zangara was found to be free of insanity at his trial and was electrocuted. Many writers have speculated about the fate of the United States during some of her most difficult years (the Great Depression, World War II) had the .32-caliber bullet from a cheap, nickel-plated revolver killed Roosevelt instead of Cermak.

Giuseppe, or Joe, Zangara was born in southern Italy on the 7th of September, 1900. At age 6, after only two months of school, he was put to work by his father. He began to resent authority, a resentment that was to assume delusional proportions in later years. Like many psychotic persons with paranoid illnesses, Zangara had a long record of psychosomatic disturbance, in his case stomach trouble. Throughout his life he blamed his ailing stomach on the fact that he had been put to work as a child. When he was 25 years old, physicians in a New Jersey hospital removed his appendix because he complained of anorexia and severe abdominal pain; the appendix, they discovered, was not inflamed. After his execution, the autopsy report noted that no gastrointestinal disease was found.

Missing the usual experiences of childhood had a strong impact on Zangara's development:

> All his life he resented it [having to start work at age 6]. He was angry at his father, but angrier yet at the "capitalists"—men, he believed, who not only withheld money from his father and thus made Joe work and ruin his stomach, but who sent their own children to school to learn and to acquire opportunities which Joe felt that he could never have. He developed a hatred for privilege. He disliked playmates whose families were better off than his, and years later he detested his officers in the Italian Army.
>
> A few days after he was removed from the classroom, he was shoveling dirt beside a road when a carriage filled with children on their way to school passed by, and the memory of their good fortune made him smart with envy twenty-five years later. In his testimony at his trial, he kept reverting to the subject of education. When he was asked what kind of change he thought a President should sponsor, he said, "I think the change is: New government. No money so everybody is same like. Everybody just the same as the country. I have no sick stomach because I have the right to go to school same as everybody else. Then the children of capitalists make no difference. All born equal. All people just the same. All people can read just the same."[1]

His extreme resentment, at first properly directed at his father, spread to capitalism as it began to become woven into his psychotic illness and then extended to the highest symbols of authority: presidents, kings, and prime ministers. All mortal rulers should be killed, he thought. Sometime about a year before he emigrated to the United States, he bought a pistol with the idea of killing King Victor Emmanuel III; a large crowd and the presence of guards discouraged him. After reaching the United States, he considered shooting President Calvin Coolidge.

Toward the end of World War I, Zangara was taken into the Italian Army, where he spent five years in hatred of his officers. Soon after his discharge he came to America, arriving in Philadelphia just before his twenty-third birthday. He moved to Paterson, N.J., to live with his uncle and work as a bricklayer. In 1924 he took out his first papers for citizenship—because membership in the union required that he do so, not because he had any feeling about the United States. He attained full citizenship at age 29, four years before he was to aim a pistol at the next President. Until 1931 he continued to live in and near Paterson, for the most part, working as a contractor for a while and in general prospering. He dressed well, sent money to his father in Italy, and bought an automobile. At one point he had accumulated $2,500. Prosperity did not alter his delusions or hostility to figures of authority.

A good worker, Zangara nevertheless spouted off during lunch hours on the privileges of the wealthy and the mean lot of the laborer. That his way of life was no longer mean made no difference. He complained about and suffered greatly from his psychosomatic gastric pain but apparently did not give any hint of the ill will he felt toward kings and presidents. He never dated; rarely drank, and then only a glass of wine; and did not smoke. Usually in bed by 9:00 P.M., "he was regarded as a mild, solitary, harmless, almost morose bachelor. As he grew older, he became so fond of solitude that once, when he was living in Hackensack, New Jersey, he rented two adjoining rooms, one to use himself and the other to make sure that nobody else

rented it."[1] Convinced that cold weather exacerbated the pain in his stomach, he stayed indoors as much as possible during the winter. "Night air" particularly frightened him.

Around 1931 Zangara's previously dormant mental illness, largely characterized by gastric complaints and unexpressed delusions, became overt. This previously industrious man lost interest in working and began to travel to warm regions, searching for health. He gave up looking for work other than odd jobs in the two years before the assassination attempt.

During the winter of 1933, while the country was suffering the effects of the depression, Zangara again thought about assassinating a President. Because of the cold in the North, however, he kept postponing a trip to Washington to kill President Hoover. He was still in Miami when he learned that President-elect Franklin Roosevelt, cruising on a yacht in Florida waters, would arrive on February 15 and give a speech in Bayfront Park. In Zangara's sick mind a President-elect, particularly in tropical Miami, was just as fitting a target as a President who, inconsiderately, stayed in the cold North. He bought a revolver and cartridges in a pawnshop.

Roosevelt was scheduled to arrive in the park's amphitheater at 9:30 P.M. Zangara thought that if he got there at 8 o'clock he would have plenty of time to get a seat in the front row, where he would be in close shooting range when the President-elect drove up. But when he arrived, not only were all the front seats filled, but the aisles were crowded as well. He pushed his way down one of the aisles in an effort to reach the front, but 15 or 20 ft. from his goal he came up against a man who resented being shoved. The man's angry words kept Zangara where he was. The smallest of all the assassins, he was not quite 5 ft. tall and weighed only 106 lb. When the open touring car in which Roosevelt was riding drove by, he could not get a clear view of his target over the taller people in front of him.

The car stopped at a stage about 30 ft. from Zangara. Microphone in hand, Roosevelt sat on the top of the back seat and gave a brief speech. When he finished, he slid down into the back seat, thus becoming a smaller target. As the crowd began to break up, a person on a chair near Zangara left. He jumped up on the wobbly chair, pointed his gun in the general direction of Roosevelt's head, and fired all 5 shots as fast as he could. None of the bullets hit the President-elect, but all caused injuries: one penetrated Mayor Cermak's lung, another entered the abdomen of a woman spectator, and each of the other 3 hit a bystander in the head. The mayor's wound was eventually fatal, and the abdominal injury was serious; the 3 head wounds were minor. To the dismay of Secret Service agents, Roosevelt ordered the driver to stop the car after it had gone a few feet, had Mayor Cermak put in it, and held the injured man in his arms enroute to the hospital. Meanwhile, Zangara was taken to jail on the trunk rack of another car in the procession, 3 policemen sitting atop him. "When he arrived there, he said repeatedly that he was sorry he had not killed the President-elect and that all he hoped for was another chance. While he was talking, he kept stroking his stomach."[1]

After his arrest and during his incarceration Zangara revealed for the first time, as far as anyone knows, all the thoughts he had kept so well concealed for so many years. He became talkative, defiant, and boastful. He would, he said, kill Mussolini and the King of England if given the opportunity. The poor of the world would benefit by his acts, he said. In passing, it is worth noting that he is one of the few assassins not to ascribe their acts to a command of God.

In court Zangara stated emphatically that he wanted no legal help. He was tried twice, once before and once after Mayor Cermak's death on March 6. After examining him in jail, two psychiatrists made a diagnosis of "psychopathic personality" but refused to pronounce the prisoner sane or insane, leaving this decision up to the court. A plea of insanity, the only possible defense, was never made. As other assassins before him had done, Zangara insisted that he was not crazy; in this case, too, nearly everyone agreed with him. "This man is unquestionably sane," said the judge in the first trial.

In 1953 Robert J. Donovan, collecting material for *The Assassins*, interviewed the younger of the two psychiatrists who had examined Zangara shortly after the attempted assassination. Speaking with hindsight and the benefit of twenty years of professional experience, the physician said: "I am sure that if [Zangara] were alive today and we had the modern facilities for examining him psychiatrically, he would have been adjudicated as a very insane person and probably hopelessly insane."[1]

Zangara was electrocuted at 9:15 A.M. on March 20, 1933, in the Florida State Prison, yet another psychotic person to pay the price of his life for his illness. He had, in my opinion, paranoid schizophrenia.

(To be continued in July)

The Use of Large Doses of Angiotensin in Acute Myocardial Infarction with Shock

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RECENTLY, an antihypotensive, angiotensin amide (Hypertensin®) (1-L-asparagioyl-5-L-valyl angiotensin octapeptide) became available for the treatment of shock and vascular collapse. A review of the literature[1–16] indicated several advantages over most available agents. Although the manufacturer does not recommend use of this agent in shock due to, or associated with, myocardial infarction, our experience shows it useful and it is the drug of our choice.

CASE REPORT

A 67-year-old male with known heart disease and severe precordial pain of one week's duration was admitted to the hospital on Dec. 10. His blood pressure was 150/90, his pulse was 110, and his temperature was 100° F. The skin was warm and moist. Auscultation of the chest revealed a protodiastolic gallop rhythm and no evidence of congestive failure. Peripheral pulsations were present. A right bundle branch block and evidence of an anteroseptal wall myocardial infarction were noted on the electrocardiogram.

The patient was given mercaptomerin and placed on heparin and warfarin sodium. During the first hospital day he experienced severe pain with weakness and cold sweats. On the following day his blood pressure was 130/78, his pulse was 124, and bilateral pulmonary rales were noted. He was digitalized and given potassium triplex. Urinary volume was 30 cc. The next day the patient was given intravenous fluids containing potassium, glucose, and insulin. Three days after admission his blood pressure was depressed and his skin was cold and clammy.

Despite intramuscular metaraminol, the blood pressure did not exceed 80/60. Hydrocortisone, 100 mg., and metaraminol, 500 mg., were added to an intravenous drip and seemed to raise blood pressure. The next day clinical shock reappeared; the patient was restless and moderately disoriented. Intravenous drip of 500 cc. glucose with 15 mg. of Hypertensin® was started. Blood pressure rose to 96/80. Protodiastolic gallop at a rate of 116 and signs of congestive heart failure continued. The patient became quiet and cooperative and his skin became warm and moist.

Later in the day signs of acute pulmonary edema appeared. Small phlebotomies were repeated. An endotracheal tube with Bennett respirator was placed. Tracheotomy was done subsequently. Despite therapy pupils remained dilated, cyanosis persisted, and gallop rhythm was marked. Pulse rose to 132, and temperature to 103.6° F. He was given acetaminophen, chloramphenicol, and nitrofurantoin. When fever did not subside, kanamycin sulfate, colistin sulfate, and vancomycin were substituted.

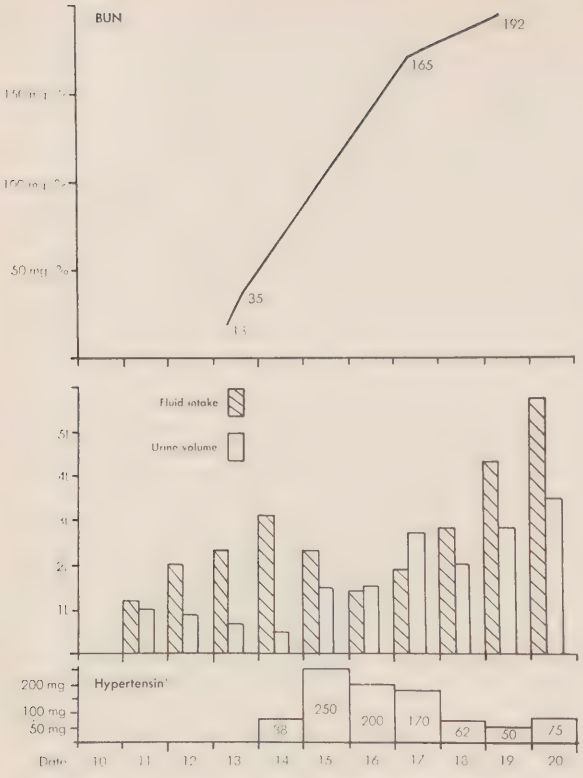
He continued to receive Hypertensin® in large doses and his condition improved. Blood pressure was maintained between 110/80 and 130/80. The dose of Hypertensin®, 250 mg., on Dec. 15, exceeded any previously reported. Each subsequent day requirements were less (see graph).

On Dec. 18 the patient felt better, took food by mouth, and was oriented. Blood pressure was maintained on lesser amounts of Hypertensin®. Urinary output was good. Heart rate had slowed to 80 beats per minute. Lungs were fairly clear. On Dec. 20 the patient suddenly became opisthotonic and cardiac arrest occurred.

LABORATORY RESULTS

Date and time	*Blood urea nitrogen, mg. percent*	*Creatinine, mg. percent*	*mEq. per liter*					
			Na	*Cl*	*CO_2*	*Ca*	*P*	*K*
Dec. 11, A.M.	18							
Dec. 11, P.M.	35							
Dec. 15			134	96	25.4			6
Dec. 17	165	4						
Dec. 18				92.8	25.5			4.95
Dec. 19	192					7.4	9.5	
Dec. 20			128.5	82.8	4.6			

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Graph showing course of BUN intake and output in relation to Hypertensin®

Provisional anatomic diagnoses at autopsy were: (1) coronary occlusion by atheromatous debris of left anterior descending coronary artery, (2) severe, arteriolonephrosclerosis, bilateral, (3) focally ulcerated erosive gastritis, and (4)bronchopneumonia, right lower lobe.

MICROSCOPIC EXAMINATION

Lungs: Bronchopneumonia. Focal atelectasis and congestive hyperemia

Kidneys: Focal areas of hemorrhages and lymphocytic infiltrate, arteriolar sclerosis

Stomach: Focal ulcerated erosive gastritis

COMMENTS AND OBSERVATIONS

The fact that this patient in shock was maintained on extremely large and previously unreported doses of Hypertensin® led us to report this case. The patient did not have the cold, clammy skin, disorientation, and decreased urinary output which sometimes accompany the use of pressor agents.

The autopsy demonstrated some congestive failure but did not show excessive fluid in the pleural cavity. The gastrointestinal tract showed some superficial ulceration which could occur with shock without the use of pressor agents. The final rise in the BUN may have been associated with the effect of Hypertensin® on the renal vasculature. However, the total urinary output did not decrease but rather was restored by the drug. Nitrogen retention had begun three days before the drug was administered (see graph).

We believe several advantages of Hypertensin® over other agents were demonstrated including the fact that it can be used in small amounts of fluid, thus obviating blood volume increases. Infiltration did not cause necrosis nor did tachyphylaxis occur.

SUMMARY AND CONCLUSION

A patient with myocardial infarction and shock was maintained for eight days on extremely large doses of Hypertensin®. No definite irreversible toxic effects were noted. It is our opinion that Hypertensin® may well be the drug of choice for shock associated with myocardial infarction.

Hypertensin® furnished by Dr. William E. Wagner, Ciba Pharmaceutical Co.

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Coexistent Sarcoidosis and Gout

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THE ASSOCIATION of gout and sarcoidosis has recently been described, but is not widely recognized.[1,2] The following case is of interest because of the onset of gout several months after the diagnosis of sarcoidosis was made, and the fact that the patient is a Negro male with no family history of gout. This case adds evidence to the likelihood that gout and sarcoid are more than casually related.

CASE REPORT

A 32-year-old man was seen in the Medical Clinic, Noble Army Hospital, in April 1963, because of a chest X-ray that showed bilateral hilar adenopathy consistent with pulmonary sarcoidosis. The patient stated he was in good health. There was no family history of sarcoid or gout. Physical examination revealed no abnormalities. Total protein was 9.04 gm. percent with albumin of 5.38 gm. percent, and globulin of 3.66 gm. percent. Serum calcium was 10.4 mg. percent, and thymol turbidity was 17.5 units. Serum protein electrophoresis was within normal limits. First and second strength PPD skin tests were negative. Skin tests for histoplasmosis and coccidioidomycosis were also negative. A second chest X-ray showed no change in the bilateral hilar adenopathy. X-rays of the hands and feet were within normal limits.

In May 1963, the patient was admitted to the hospital where a right scalene lymph node biopsy was performed. The pathologic diagnosis of that specimen was noncaseating granuloma consistent with sarcoidosis.

The patient continued to be asymptomatic until July 28, 1963, when he awoke with excruciating pain at the first metatarsal phalangeal joint on the right. Physical examination at that time was negative except for swelling, redness, and extreme tenderness about the first metatarsal phalangeal joint on the right. A chest X-ray taken during this admission showed a moderate decrease in the hilar and mediastinal nodes. X-ray of the right foot was negative. Uric acid on admission was 12.2 mg. percent, the BUN was 8.5 mg. percent, the fasting blood sugar was 120 mg. percent, the calcium was 11.2 mg. percent, and the phosphorus was 3.0 mg. percent. Serological test for syphilis was negative. Urinalysis and complete blood count were within normal limits. Total protein was 10.1 gm. percent, with an albumin of 5.9 gm. percent, and a globulin of 4.2 gm. percent. Twenty-four hour urinary excretion of calcium on a normal diet was 130 mg. Serum protein electrophoresis was within normal limits. The patient was initially treated with an hourly dose of 0.5 mg. of colchicine until the pain subsided, which was about sixteen hours after admission. He was also placed on 0.5 gm. of probenecid twice daily and on a high fluid intake. On this regimen he rapidly became completely asymptomatic. A second uric acid was 8.0 mg. percent and a uric acid just prior to discharge was 6.6 mg. percent. The patient was discharged on a low purine diet, 0.5 gm. of probenecid twice daily, and a high fluid intake.

He remained well until Nov. 4, 1963, when he again developed pain in the first metatarsal phalangeal joint on the right. Two days after onset he was readmitted to the hospital. Physical examination was again within normal limits except for redness and tenderness over the lateral aspect of the right first metatarsal phalangeal joint. Uric acid was 4.8 mg. percent. Urinalysis was within normal limits. Complete blood count was within normal limits. Serological test for syphilis was negative. The patient was treated with 0.5 mg. of colchicine every hour until his symptoms were relieved. At this time the patient developed some diarrhea. He was kept on a maintenance dose of 0.5 mg. of colchicine three times a day, plus continuing the 0.5 gm. of probenecid twice daily. He was discharged six days after admission, completely asymptomatic. A chest film taken during this admission showed the hilar shadows to be essentially unchanged.

The patient has remained asymptomatic up to the present time. A uric acid determination on Jan. 14, 1964, was 10.4 mg. percent; uric acid

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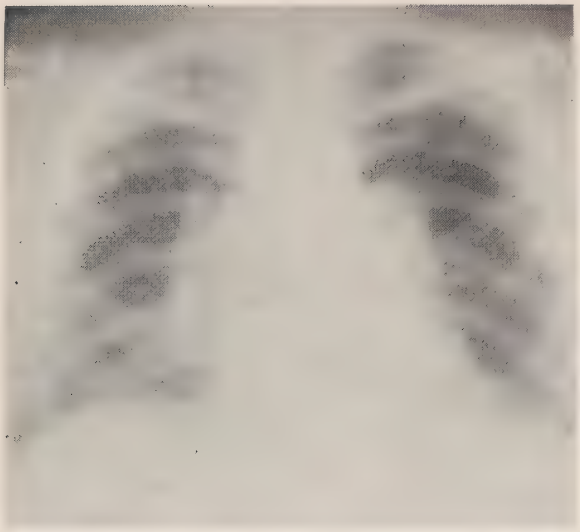


Fig. 1. Chest X-ray taken April 1963 showing bilateral hilar adenopathy

drawn on Jan. 22, 1964, was 7.2 mg. percent. On March 27, 1964, the total protein was 8.5 gm. percent, with albumin of 5.5 gm. percent, and the globulin was 3.0 gm. percent. Calcium was 10.8 mg. percent, phosphorous was 3.6 mg. percent, and the uric acid was 6.4 mg. percent. The chest X-ray again demonstrated hilar prominence. He continues to be on probenecid and colchicine.

DISCUSSION

The fact that an elevated uric acid level may be associated with sarcoidosis has been known for some time, but has not been widely appreciated.[3] It has only been recently, however, that sarcoidosis and gout have been described in the same patient, although one of these cases was also associated with psoriasis which is itself a potential source of hyperuricemia.[4]

That this patient had gout is established on the basis of a classic clinical picture and the elevated serum uric acid levels. Similarly, the diagnosis of sarcoidosis seems secure in the face of the X-ray and biopsy findings, plus the negative skin tests. The patient had no family history of gout and is a member of a race that has a low incidence of primary gout. Also, the high uric acid level of 12.2 mg. percent that this patient initially had is more consistent with secondary than primary gout.[5] Thus, this case would seem to reinforce the possibility that sarcoidosis may be a cause of secondary gout.

This case, and the others previously described, would suggest that all cases of sarcoidosis should have serum uric acid determination and that

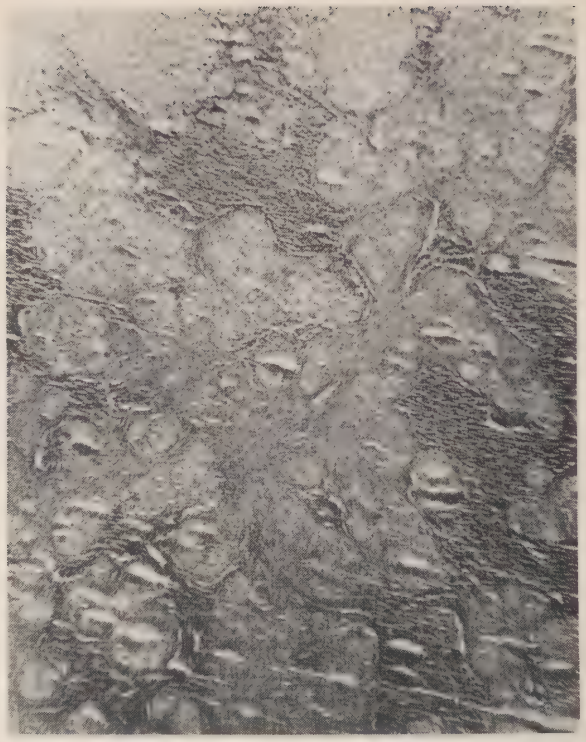


Fig. 2. Photomicrograph of scalene node showing multiple, small, discrete, noncaseating granulomas. × 100

sarcoidosis be added to the differential diagnosis of secondary gout.

SUMMARY

A case of classic podagra occurring in a 32-year-old Negro male several months after the diagnosis of sarcoidosis was made is described. The association of gout and sarcoidosis is stressed. The advisability of serum uric acid determinations in all patients with sarcoidosis and the inclusion of sarcoidosis in the differential diagnosis of secondary gout are mentioned.

This material has been reviewed by the Office of the Surgeon General, Department of the Army, and there is no objection to its presentation and/or publication. This review does not imply any endorsement of the opinions advanced or any recommendation of such products as may be named.

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Chronic Disease Research

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I DEEM IT A PRIVILEGE to have been granted the latitude implied in a title of such breadth as "Chronic Disease Research." The privilege fortunately provides license of selection in an area of such diversity and complexity. Rather than attempt a cataloging of current research in this area it would be preferable to examine some general aspects of the chronic degenerative diseases and the patterns of approach to their research. In this way a humble beginning may be made toward an understanding of the details of such research and the problems of their interpretation.

The chronic diseases present certain characteristics which contribute to the difficulty of their study. Two features of importance are immediately apparent: a prolonged latent or induction period, and an insidious onset of signs and symptoms. The latent or induction period is analogous to the incubation period of the infectious diseases but is designated otherwise to avoid the *a priori* conclusion of infective agents as causes of these chronic diseases. Parenthetically it should be noted that although in some cancerous lesions of animals viral agents have been implicated, none have thus far been established for man. Furthermore, the viral theory of cancer production in man would include, in our present state of knowledge, collateral but necessary activating agents or "triggers." These activators may be certain environmental substances, called carcinogens when they have been demonstrated to cause cancer. The induction periods in chronic diseases, unlike the incubation periods of infectious diseases, are frequently very prolonged—some being as long as twenty years or more. It is not always clear whether the length of the induction period is a reflection solely of a dose-time relationship, for example, the accumulation of effects from repeated or continuous low-dose assaults, or whether it represents the time necessary for the developing pathologic process to manifest itself sufficiently for observation, or both. At this point it must be interjected that the length of the induction period is not known for the greatest number of the chronic, so-called degenerative, diseases. It is a rare opportunity to associate a dramatic event such as the Hiroshima bomb with the peak development of excess leukemia cases in the exposed population seven years later. Where research has implicated causal or contributory factors in the production of a chronic disease these have been found to have acted, or at least begun to act, on the individual a number of years earlier. From such observations it is assumed that most, if not all, chronic diseases have relatively long induction periods.

In any event, this prolonged induction period makes it difficult to ferret out causal factors. Once a diagnosis has been made, the antecedent events may be obscured by antiquity. It is a far cry from relating a number of cases of gastrointestinal distress to a common school lunch one-half hour before, or to a church supper two or three days previously. Those who have investigated typhoid outbreaks have been faced with the serious problem of having patients recall their activities of three or four weeks earlier. The case of rheumatoid arthritis may theoretically have had predisposing infections of ordinary bacterial or viral agents thirty to forty years earlier; the case of pulmonary emphysema may have had its causal factors operating years earlier.

The insidiousness of the onset of the chronic degenerative diseases also contributes to the problem of their study. Unlike the acute infectious diseases with their dramatic, virtually sudden onset, the chronic diseases may provide only a few signs and still fewer symptoms below the level of serious discomfort so that medical care

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is not sought. When surveys of prevalence or research on causality are mounted in population groups our levels of diagnostic precision may leave much to be desired for diagnostic classification early in the disease. In acute infectious diseases—or even the chronic infectious diseases such as tuberculosis, syphilis, or leprosy—a highly specific test such as isolation of the responsible pathogenic organism may be applied at onset. Insidiousness of onset also aggravates the problem of attempting to associate the disease with certain antecedent factors which may be causal. A diagnosis may, of necessity, be delayed beyond the time of recall or past the opportunity for objective observation of the factor, at least in relationship to that individual case. For example, in nitrogen dioxide poisoning bronchiolitis fibrosa obliterans, a slowly strangling plugging of the small airways of the lung by fibrous connective tissue induced by the chemical trauma, has an insidious onset. This obviates the measurement of the level of NO_2 in a silo or chemical laboratory, responsible for the disease when that level of exposure was experienced three to four weeks earlier and the atmosphere dissipated in the meantime. Thus, insidiousness of onset is tactically a part of the problem posed by the length of the induction period.

A third characteristic posing problems in the study of chronic degenerative diseases, and particularly their causes, is their usual association with older age groups in the population. This concomitance may obscure the roles of environmental factors among the more nearly inherent physiologic processes of aging. When such diseases also occur in the young, though much less frequently, we immediately suspect factors other than aging.

An additional characteristic is actually true of all biological phenomena, though it achieves its highest expression in the chronic "degenerative" diseases. This is the existence of multiple causative factors for each disease. This has at least two facets which may fuse subtly. A disease may have a necessary condition but this condition may not be sufficient for the production of the disease. Tuberculosis and diphtheria are two disease examples in which the tubercle bacillus and diphtheria bacillus are necessary for the production of the two respective diseases. They are not sufficient for such disease production, however, since we have many more instances of infection with these agents in the host but without the development of disease. Other factors, such as malnutrition or stress, may be important in tuberculosis. Underlying genetic susceptibility may in itself not produce other diseases, but may increase the likelihood of a given agent, such as a specific microorganism or chemical, producing a specific disease. The second facet involves the concept of the existence of multiple causative agents of a single disease. Whereas diphtheria, as we have defined it clinically and bacteriologically, is caused by the specific diphtheria bacillus, lung cancer is caused by the inhalation of substances derived from the burning of tobacco and the inhalation of chromates, nickel compounds, and probably uranium dusts and asbestos, to name but a few of the more firmly associated agents. Multiplicity of cause has its impact on both the patterns and degree of difficulty of approach to the study of a chronic "degenerative" disease. When several factors exist in the host or his environment and several agents coexist in the environment, it is not easily determined which are necessary and sufficient agents, which are necessary but not sufficient agents, and which factors are sources of variation but not causes (modifiers).

Our preoccupation with cause is not a fetish! The determination of cause has as its goal the prevention of disease. Admittedly, the determination of cause may at times prove to be idealistic; that is, the removal of the cause may be impossible or at least impractical. Frequently, determination of cause in the formalistic sense (when, for example, the factor is found to be both necessary and sufficient) fails, but factors are elicited which, as they increase or diminish, are associated with fluctuations in the incidence of the disease. The pragmatic concept of causality would include such factors as causal. It has already been pointed out that in biological phenomena the requirement that a factor be both a necessary and sufficient condition need not be met for the incrimination of a cause because of the existence of multiple causative factors and particularly where multiple causative agents exist. My emphasis today on the epidemiologic approach to research in the causes of chronic disease is not based on personal preferences of a vocation but on a number of considerations. Since epidemiology, the basic science of public health and preventive medicine, is defined generally as the study of the mass phenomena of disease or of the distribution of disease in populations and, more specifically, as the study of the factors influencing this distribution, its concern with cause is inherent.

The epidemiologist is concerned with any variation in the incidence or prevalence of a disease according to its secular or long range and its seasonal cycling. He is interested in variations of occurrence on a geographic basis

whether it be among countries, states, or smaller political subdivisions such as towns or rural areas. His concern is even greater for differences of occurrence among different age groups, races, and socioeconomic and occupational groups and between the sexes. The differences in frequency which he may observe will lead him to the development of hypotheses to explain such differences. If he observes a decline or an increase of a disease in time, he may look for a concomitantly declining or increasing factor—more realistically in the environment than in the host. If he notes differences in the incidence or prevalence of disease among several countries or localities or between rural and urban communities, he may look for differences in environmental factors or in host habits leading to different exposures or risks to account for them. If he observes differences in the frequency of disease between the sexes, he may hypothesize differences in exposure or hormonal influence. One could continue to elaborate, but the point to be emphasized is that the epidemiologic method seeks to establish statistical associations between a disease and various features or characteristics of the population and its environment, and then attempts to derive hypotheses or inferences with biological meaningfulness from these associations.

With the elaboration of an hypothesis more detailed epidemiologic studies are designed to provide support for the hypothesis or to carry it to finer meaning and particularly toward a causal hypothesis. For example, an initial observation may be made by a clinician that most of the women with breast cancer that he sees "seem to be" either single women or women with no or few children. At this point an hypothesis might be developed which would entertain an influence of pregnancy or pregnant-state hormones as a preventive for breast cancer. An epidemiologic field study would be designed to check out this initial observation and determine whether it is consistent with the total distribution of this disease in the population. It would be found that this impression is indeed correct—a statistical association does exist in the population. At this stage an even more biologically meaningful hypothesis might be entertained. Nonpregnant females menstruate more or less rhythmically. Their breasts undergo constant recurring rhythmic swelling and regression. Pregnancy induces a halt to this cycling. The birth of the fetus produces an increase in the lactation hormone from the pituitary which induces lactation. Lactation continues for as long as nursing proceeds. Lactation or the lactotropic hormone may thus be protective against breast cancer. An epidemiologic study to test this hypothesis could include women who had given birth to varying numbers of children and, even more refined, women with varying durations of lactation, numbers of lactating episodes, and length of the interval between such episodes.

Another example, illustrative of the method and its yield, is that of cancer of the cervix uteri. It is observed that Jewish women have far less cancer of the cervix than non-Jewish women. This is an example of statistical association between a disease and an ethnic characteristic of the population. A genetic hypothesis might be entertained. This would be extremely difficult to support. A simpler hypothesis might involve a biological mechanism closer to the locale of action: cervical infections, size of families, lacerations of the cervix, frequency of intercourse—each hypothesis could be explored individually or collectively, taking care that proper classes of women with the varying attributes or characteristics are established for comparison by techniques to be described later. None of these characteristics would satisfactorily explain the difference in risk for cervical cancer between Jewish and non-Jewish women since, for example, in both groups the size of families and the occurrence of lacerations would have associations with cervical cancer but the differences in the proportion of these characteristics between the groups would not be found to be great if Jewish and non-Jewish women of similar socioeconomic class distributions were used. This would verify associations between size of family and occurrence of lacerations and cervical cancer but would not explain the ethnic difference. Another hypothesis must be entertained. Jewish women are married most frequently to men who are circumcised. Would the existence of the prepuce and its greater quantity of smegma production have an influence on cervical cancer rates? We would compare non-Jewish females married to circumcised males with similar females married to uncircumcised males for cervical cancer frequency; or, we could more easily look for the proportion of non-Jewish cervical cancer cases who are married to circumcised males as compared to the proportion of non-Jewish controls without cervical cancer married to circumcised males. Further refinements would be comparative studies utilizing unmarried women and finally female celibates. This has been done and the association thereby strengthened.

At this point it may be asked: "Is there not a more direct way of establishing an association between a disease and a characteristic of the

host or his environment?" The obvious answer is a properly designed human experiment which could not only provide direct proof of an association but also its causal nature. If one could select samples of persons from the population and randomly allocate them to two groups, one to which a factor is to be applied and the other from which the same factor is to be withheld, the occurrence of a much greater amount of disease in the first group than in the second would constitute proof of the causal nature of the applied factor. Such experiments are rarely feasible. It is certainly quite impractical to attempt an experiment in man to test, for example, whether a causal relationship exists between smoking of tobacco and lung cancer. Such an experiment would imply the random selection of very young subjects, living under environmental conditions as nearly identical as possible to avoid confounding by other variables, and randomly allocating them to two groups, one of which would be made to smoke and the other to serve as nonsmoker controls. Their smoking and other habits would need to be held constant for many years. Because of the relatively low incidence of lung cancer in the human population, both the test and the control groups would have to be extremely large. Thus, the impracticality of such an experiment is immediately obvious.

The epidemiologic approach to the determination of statistical associations between a disease and certain characteristics of the human population must, out of practicality, be applied to naturally occurring phenomena. Unlike an experiment, the investigator has no direct control over other possible factors that may influence the associations. Nature is performing the experiments in highly complex fashions which tax the ingenuity of man to unravel. If there were but a single cause for every disease and a 1-to-1 relationship between a factor and the disease, that is, every case of the disease had the factor and every person with the factor had the disease, there would be no need for experiments nor for other epidemiologic approaches to determine causality. The fact would quite rapidly have thrust itself on our consciousness. The necessary and sufficient condition would indeed be present and self-evident.

Multiple causality and modifying factors, however, preclude such simplicity as has already been pointed out. No one case of illness can establish a causally meaningful association with a host or environment characteristic. What characteristic do we select? He has many of them. Shall we select the one which fits our imaginative fancy? This is wishful thinking! A person working in a lead factory develops lung cancer. This is no more proof of the association between lead and lung cancer than between pregnancy and arsenic for the female who works in an insecticide factory. Can a collection of cases help us? Sixty-five percent of men over 18 years of age with ingrown toenails smoke cigarettes. Is smoking of cigarettes a causal factor in 65% of them and in 35% are other factors operating? What meaning can this have when 65% of all men over 18 years of age in the general population smoke cigarettes?

It is now obvious that in the establishment of statistical associations for the elucidation of etiologic factors, we must ultilize more or less formalized epidemiologic approaches. This may take the form of studies of demographic data in which vital statistics reports provide the data of morbidity or mortality by certain characteristics. A disease may be noted to have a concentration by certain of these characteristics and thus provide a clue for more detailed investigation.

The more formal approaches which are more likely to reflect biological relationships involve the study of individual case history data. This can be in the form of a retrospective study in which a group of cases of a disease is compared with a properly selected group of persons without the disease—known as controls—in respect to the percentage of individuals in each group who have a characteristic deemed to be a possible etiologic factor. If the group of cases have a statistically significantly higher percentage of the factor than the control group the factor is said to be associated.

Another form of individual case history study is the prospective study. Here a selected population is divided according to the presence or absence of a characteristic deemed to be a possible causal factor and each group is followed for the development of the disease in question over a definite period of time. If the group with the factor has a significantly higher risk of developing the disease than the group without the factor, the factor is said to be statistically associated.

Although both the retrospective and the prospective methods have their advantages and disadvantages, the prospective method provides a direct estimate of the risk of developing the disease when the suspected factor is present. It also provides a direct calculation of a morbidity or mortality ratio, that is, the ratio of disease produced with the factor present to that produced with the factor absent. This provides a measure of both the strength of the association and its specificity.

Epidemiologic studies short of direct experi-

mentation with human population groups have been maligned by some groups—and these almost always representing vested interests—as being "only statistical." The implication is that causality can never be inferred from statistical associations. Such individuals and groups overlook the fact that even experiments need not represent "proof" of causality in the strictest sense, for here also a judgment that the outcome of an experiment is the effect of the manipulation applied must also be made. Statistical methods cannot establish proof of a causal relationship in an association. The causal significance of an association is a matter of judgment which goes beyond any statement of statistical probability. To judge or evaluate the causal significance of the association between an attribute, characteristic, or factor and the disease or effect on health, a number of criteria must be utilized. None of these criteria is an all-sufficient basis for judgment.

The first of these criteria involves the consistency of the association. Do all or a majority of the studies reveal an association? If they do, and particularly if the methods of approach varied quite a bit, this is in favor of causality.

Another criterion is the strength of the association. This can be measured directly by the ratio of the disease rate for persons with the characteristic suspected to be causal to the disease rate for persons without the characteristic, that is, the morbidity or mortality ratio. The higher the relative risk ratio the more likely the association is causal. In lung cancer, for example, the ratio of the rates among cigarette smokers as compared to nonsmokers averaged about 9.0 for the 7 prospective studies. This actually means a 900% greater risk for smokers of cigarettes. Thus, smoking would appear to be important in this disease.

A third criterion deals with specificity of the association. This cannot be entirely dissociated from the concept of the strength of the association. This criterion implies the precision with which the disease will predict the presence, in the case, of the factor reputed to be causal. If the relative risk ratio as described above is high, this is in favor of causality. For example, in the lung cancer–cigarette smoking relationship the risk ratio is 9.0 on the average, that is, the risk among such smokers is 9 times that of nonsmokers. Since more than 50% of the population smokes, this means also that, given 10 patients with lung cancer, 9 would be smokers, that is, 90% of the cases smoked. Thus, only 10% did not smoke and in these patients other factors must be sought for. It can be concluded that cigarette smoking is highly specific for lung cancer. On the other hand, a relative risk ratio of 1.8 indicates the risk of disease among smokers is somewhat less than twice that among nonsmokers. This implies that, given 28 cases of a disease, 18 of them would be smokers, that is, 64% of the cases smoked; 36% did not. Thus, specificity of smoking for this disease is considerably lower and not too helpful in a judgment of causality.

A fourth criterion is that of the temporal relationship between the characteristic and the disease. This implies that the factor suspected to be causal must be an antecedent in time to the disease. Obvious though this may be, it is not always simple to evaluate, for it must be recalled that the induction period of chronic diseases may be prolonged and the actual injury to the cells may have taken place before the factor being evaluated became associated with the host.

The last criterion in a judgment of causality of an association is that of coherence of the association with the known facts in the natural history and the biology of the disease. Here the biologic meaningfulness of the association comes into play as well. A causal hypothesis is easier to accept if it makes biologic sense; for example, the inhalation of cigarette smoke does bring the suspected agent or agents to the tissues involved in lung cancer, chronic bronchitis, laryngeal cancer, and emphysema. Here, too, the dose-response becomes important. If a factor is causally related, the effect should increase in magnitude as the factor increases in strength. Confirmation by animal experimentation does not constitute definite proof for it is always dangerous to extrapolate from one species to another. However, such confirmation serves a dual purpose: It increases the biologic reasonableness of a causal inference from an association, and it provides a model from which biologic mechanisms may be elicited and sought for in man. Finally, the causal hypothesis must be coherent with the other epidemiologic features of the disease and the characteristic under test. If a factor is to be deemed causal for a given disease and it is present in greater proportion in a given population segment, that segment should have a higher frequency of disease and vice versa.

These, then, are the principles and methods of study of the chronic diseases. They reached their highest expression of evaluation in the recent Advisory Committee Report on Smoking and Health. The usefulness of the epidemiologic approach to ferreting out causal factors in chronic disease has again been demonstrated.

This paper was presented at College Institute on Public Health Problems, Gull Lake, Minnesota, June 1964.

Basic Neurophysiologic Aspects of Epilepsy

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EPILEPSY IS CHARACTERIZED by a state of hyperexcitability of the central nervous system. In many instances there is no demonstrable pathological abnormality, consequently this condition can be classified as a physiological abnormality of the brain. The following is a brief summary of some of the more pertinent information concerning the basic neurophysiologic concepts of epilepsy. It is beyond the scope of this paper to give the intricate details of the different aspects of this subject.

THE EPILEPTIC NEURON

The neuron is the basic element of the nervous system, therefore it seems reasonable that information could be obtained from studying individual or neuronal aggregates which exhibit hyperexcitability.

Phylogenetic developmental aspects of epilepsy. Seizure susceptibility increases with phylogenetic development; the lower the animal is on the phylogenetic scale the less susceptible it is to seizure activity and convulsions. The more primitive vertebrates such as the cyclostomes and fish will exhibit only a clonic type convulsion with some locomotor effect. The amphibian will exhibit the two basic motor components, the clonic-tonic convulsion, but these are not characteristic and are mixed with primitive locomotor elements. Reptiles are the lowest vertebrate that will exhibit convulsions beginning with the initial clonus, followed by the tonic phase and the terminal clonic phase. Mammals are born with a low seizure susceptibility, but susceptibility increases rapidly within the first few days or months until the first or second year. It then decreases except for the period of puberty when susceptibility increases.[1] Tonic phase of the convulsion decreases as the brain develops and the immature brain resists the evolution of the tonic-clonic sequence of generalized convulsions in favor of the limited tonic contraction. Consequently pure tonic seizures are seen in small children or in cases of diffuse cerebral disease.[2]

The development of seizure susceptibility in the young can be correlated with the maturation of the nervous system. Early in development the cells are arranged in vertical columns with the dendrites projecting off the apical end and axonal projections off the basal end of the cell body in a vertical fashion. At this time there is a poverty of horizontal collaterals between the neurons. Thus the cortical discharge will spread vertically more readily than horizontally. In the adult, horizontal collaterals have developed bringing about interactivity between the neurons.[3] Such an arrangement is beneficial for the production of synchrony of discharge which is essential in an epileptic seizure and makes the neuronal network more susceptible to a seizure. The horizontal collaterals also contribute to the inhibitory clonic component of the clonic-tonic phase. Thus in the early stages of development there is a lack of horizontal collaterals and seizure susceptibility is low. As the collateral system develops, synchrony between neurons increases and seizure susceptibility increases.[3]

Electrical activity of the epileptic neuron. Seizure discharge is characterized by high voltage activity. This activity may be related to the following four factors: (a) Total number of active neurons, (b) The degree of synchronization of a unit discharge, (c) The degree of depolarization of each cell since cell potentials do not obey the all-or-none law, and (d) The orientation of the voltage gradients in each cell relative to the recording electrode.[4] Thus an increase in voltage may be due to more neurons firing, or a greater synchronization between the firing units with no increase in the number of cells involved, or a higher potential across the cells, or a combination of these.[4]

The ability to discharge at high frequency is not, of itself, an abnormal neuronal characteristic. Some sensory neurons, when stimulated by physiological means, will fire at a rate up to 1,200 per second. The factor which distinguishes

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the epileptic neuron from the normal is its ability to fire spontaneously at high frequencies and to maintain this burst discharge for long periods of time. This hyperexcitability is due to a change in the internal environment resulting from a change in membrane permeability.[5]

During excitation or depolarization, there is an increase in the permeability of the cell membrane resulting in a movement of sodium and water into the cell.[6] When the membrane of the dendrites and soma of the neuron become sufficiently depolarized the cell discharges an impulse, consequently the amount of depolarization determines the activity of the cell. An increase in the amount of depolarization will produce repetitive firing while excess depolarization produces a state of hyperpolarization which inactivates the cell.[7] The epileptic neuron appears to be in a state of relative enduring dendritic depolarization which results in spontaneous discharges over long periods of time. It has been postulated that mechanical deformation of the dendrites by fibroglial scar tissue is responsible for the increased depolarization.[8]

Another possible mechanism of neuronal hyperexcitability involves the epileptic focus. This consists of an aggregate of epileptic neurons and is characterized by a negative potential of an appreciable magnitude. It is possible that current flows from the adjacent cortical tissue into this negative sink resulting in hyperexcitable neurons.[8] Experimental evidence has demonstrated that epileptic neurons are hyperexcitable, however, the reason for this remains obscure.

There is no constant relationship between the discharge pattern of single neurons in a focus and the slow surface events recorded on the electroencephalogram. Morrell noted that one unit exhibited a high rate of discharge unassociated with surface paroxysmal activity, while neurons 100 μ away were inactive.[9] The epileptic spike as recorded on the electroencephalogram is presumed to be a consequence of variations in the magnitude and proportions of depolarizing, excitatory and hyperpolarizing, inhibitory postsynaptic potentials generated in neurons in complex synaptic organization.[10]

It is apparent that the neuron must be regarded as a major unit in seizure production. The epileptic neuron is hyperexcitable and has increased spontaneous activity including a greater response to afferent impulses. This hyperexcitability is possibly due to a change in cell membrane permeability which may result from enduring dendritic depolarization. The slow surface activity observed on the electroencephalogram is not due to any single neuronal event but results from the summed total activity of many neurons which make up an epileptogenic focus.

THE EPILEPTIC BRAIN

This section will be concerned with the effects of the epileptic discharge upon the whole brain, considering the possible sites of origin, mechanisms of spread of the discharge, and convulsive activity.

Sites of origin. Epilepsy can be classified as generalized or partial depending upon the extent of cerebral involvement. The extent of involvement is dependent, in part, on the site of origin of the focus. It has been stated that generalized seizures originate as the result of a subcortical pacemaker and the discharges are propagated to both hemispheres in a diffuse manner producing abnormal electrical activity of the cerebral cortex which develops simultaneously in all cortical areas. Such a pacemaker would have to have widespread and functional connections to the entire cortex.[11] Many believe that the site of origin of generalized seizures is located in the diencephalon, cephalic reticular formation, and thalamus from which the term centrencephalic epilepsy arises.[4] The origin of certain aspects of the electrical activity, such as the typical spike and wave pattern recorded on the electroencephalogram, has been studied. It has been concluded that the spike is of cortical origin in response to the slow wave which is of thalamic origin.[12,17] Penfield states that petit mal, myoclonic petit mal, and grand mal seizures all have their origin within the centrencephalic system.[4]

The site of origin of partial epilepsies is usually limited to a specific area and may arise from brain pathology such as scar tissue or tissue damaged by anoxia. This last condition is associated with traumatic head injuries during birth at which time the blood supply to areas of the temporal lobe region is impaired. The extent of the seizure arising from a limited focus will depend upon the location of the focus. Seizure activity may occur without any clinical manifestations and may be observed only as a local electrographic abnormality. Focal sites in the motor cortex may produce a limited convulsion depending upon the exact location of the lesion, while in other cases localized foci may give rise to psychomotor disturbances producing widespread manifestations. This is especially true of temporal lobe epilepsy.[12]

Another type of localized lesion is the secondary focus. This develops from the continuous activity of a primary lesion on an area which is

anatomically allied to the primary lesion, usually being located in the opposite hemisphere. The secondary focus is dependent on the activity of the primary lesion in the early stages, but may become independent of the primary lesion in due time. Early removal of the primary focus is essential for the elimination of a secondary focus.[13]

All partial epilepsies may become generalized, especially if the discharge originates in an area where neurons are hyperexcitable or that exhibits a low convulsive threshold, such as the hippocampus or precentral motor area. Certain factors appear essential in order for a localized seizure to become generalized. These include the rapidity of the attack and the structures involved. The more rapidly the attack occurs, the more likely for it to become generalized; also if the structures involved have numerous connections, the greater the possibility of spread.[14]

Mechanisms of spread. There appear to be three major mechanisms or routes of spread of an epileptic discharge. In generalized seizures the abnormal activity which is presumed to originate in the diencephalon and reticular formation passes to the cortex via the thalamocortical projections and produces extensive bilateral dysrhythmia.[2] Activity arising from cortical epileptogenic foci spreads to the surrounding cortex by the slowly propagating intracortical or intercortical pathways as in a Jacksonian march.[15] The third mechanism is via the large, fast fibers of the commissural connections, especially the corpus callosum, which transmit impulses from an epileptogenic focus in one hemisphere to the homotropic site in the other hemisphere. This discharge is propagated by means of normally functioning nerve fibers from an epileptogenic focus to the corresponding area in the other hemisphere and is involved in the production of a secondary focus.[13] It should be mentioned that localized cortical foci can produce diffuse, bilateral epileptiform activity which is mediated through the midline thalamic reticular formation. This is primarily observed in lesions of the cingulate gyrus.[16]

Mechanism of convulsions and seizure activity. The actual mechanisms involved in the production of the epileptic attack are unknown; however, several theories have been postulated using the available information. Gastaut believes that the brainstem reticular formation is responsible for both the abnormal electrical activity and convulsion. The caudal portion produces the convulsive activity and the rostral portion produces the seizure activity of the cortex which results in unconsciousness. Tonic spasms and clonic convulsions depend upon the facilitatory influence of the caudal reticular formation on the motor neurons of the cord. The cortex and higher centers under normal conditions inhibit this activity of the reticular formation which results in normal muscular tone (Fig. 1); however, when the cortical influence is removed reticular facilitation predominates. This can be observed in decerebrate rigidity where a section through the midbrain removes the inhibitory activity of the higher centers resulting in increased facilitation and rigidity. In a generalized epileptic fit, discharges from the epileptic focus in the midbrain are transmitted to the cortex via the thalamocortical paths producing unconsciousness and dysrhythmia of the cerebral electrical activity resulting in a nonfunctional cortex and higher centers. The exclusion of this thalamocortical system liberates the caudal reticular formation from the inhibitory influence and results in increased facilitation and convulsions (Fig. 2). Thus, the caudal reticular formation is responsible for the convulsive activity and the rostral

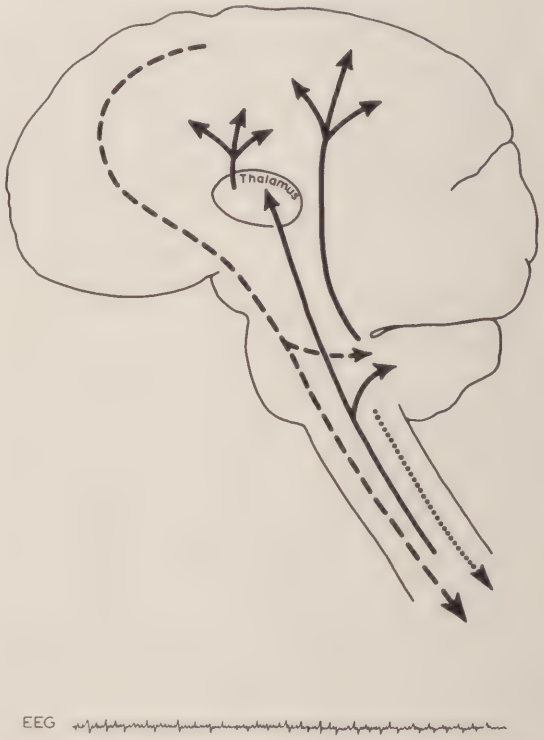


Fig. 1. This illustrates the normal brain. Solid arrows indicate ascending impulses to the midbrain, thalamus, and higher cortical centers resulting in a normal EEG and consciousness. Dashed lines demonstrate cortical inhibitory influence on the midbrain and motoneurons of the cord while the dotted lines indicate midbrain facilitating influence on the motoneurons of the cord. Cortical inhibition on the midbrain results in decreased facilitation on motoneurons of cord producing good muscle coordination. (Modified after Gastaut)

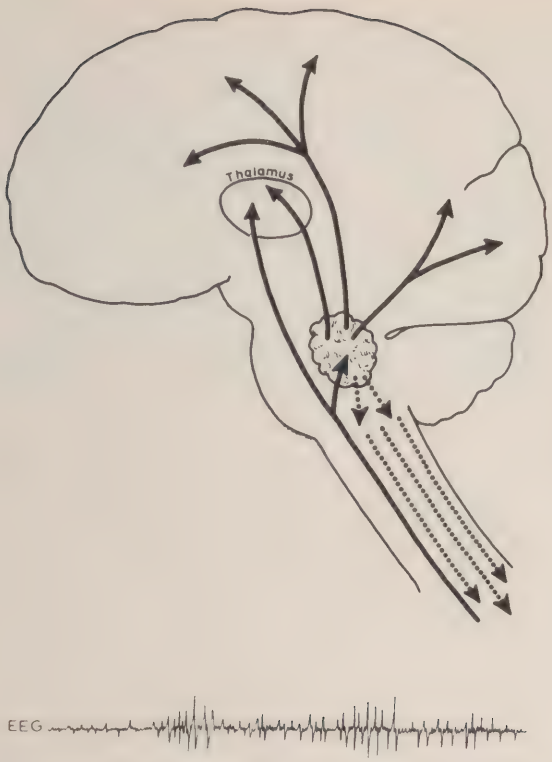


Fig. 2. This illustrates an epileptic brain. Epileptogenic focus in midbrain eliminates normal thalamocortical activity resulting in seizure activity, as demonstrated by the EEG trace, and unconsciousness. The lack of cortical inhibition upon the caudal reticular system accompanied by an increase in midbrain facilitation due to the epileptogenic focus activity results in convulsive movements. Dotted lines indicate midbrain facilitation on the motoneurons of the cord. (Modified after Gastaut)

reticular formation for the abnormal electrical activity and unconsciousness.[17] This theory has not been substantiated in the laboratory.

Experimental studies concerned with the role of the reticular formation in convulsive activity tend to minimize the reticular control. Walker concluded that lesions of the reticular formation do not alter the pattern of focal or generalized seizures, although the reticular formation did modify the excitability of the cerebral cortex.[18] Other studies referred to in this paper state that the reticular formation actually suppresses induced seizure activity.

The role of the cortex in convulsive activity is also controversial. There is evidence that seizures can be evoked in the absence of the cortex or upper brainstem which demonstrates the seizure potential inherent in the lower brainstem. Experimental studies have demonstrated that ablation of the cortex produces a marked depression of the myoclonic response and it was concluded that the motor cortex contributes significantly to, but is not indispensable for, the development of myoclonic and generalized seizures.[19] This is contrary to Gastaut who claims that the absence of a functional cortex results in the clonic-tonic aspect of a generalized seizure.[17] It would appear that if the motor cortex was involved in the production of convulsive movements, this activity would be transmitted by way of the corticospinal tracts, and if such tracts were destroyed the convulsive activity would be eliminated. Merlis states that cortical activity in evoked myoclonic and generalized seizures is mediated largely, but not exclusively, by the corticospinal paths which exert a facilitatory action on flexor mechanisms of the spinal cord.[19] Gastaut claims that seizures which are generalized from the start are not cortical in origin or propagated by the corticospinal tracts.[17] Walker states that the corticospinal tract plays a secondary role to other descending pathways in transmission of the epileptic discharges from the cerebrum.[20] It is apparent that a definite statement can not be made from available information concerning the role of the cortex or reticular formation in a generalized seizure.

In partial seizures, the convulsive activity will depend upon the location of the lesion. If the epileptogenic focus is confined to an area of limited connections, the resultant convulsion will be limited. This is especially true of cortical lesions located in areas such as the precentral gyrus which projects to the ventrolateral nucleus of the thalamus and will induce clonic jerks. Lesions of the geniculate will induce localized visual disturbances. If the causal discharge originates in an area with diffuse connections the resultant action will be of greater magnitude. Seizure activity originating in the rhinencephalon, such as the amygdala, induces vegetative manifestations involving epigastric, abdominal, and precordial sensations.[17]

It is evident, after reviewing the literature, that the basic aspects of epilepsy are not known. There are many controversial issues, both major and minor, which demonstrate the lack of comprehension of this problem; however, it should be emphasized that many aspects of normal brain functions, such as the electrical activity of the brain, are not completely understood, which makes it much more difficult to understand the pathological processes. This lack of understanding of the mechanisms of epilepsy is detrimental to the advancement of the therapeutic aspects.

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So-Called Alveolar-Cell Carcinoma of the Lung

Report of a Case

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ALVEOLAR-CELL CARCINOMA of the lung is a rare disease. This is a case report of an alveolar-cell carcinoma simulating a miliary tuberculosis of the lung.

A 66-year-old woman was admitted in our clinic on Jan. 27, 1963, with anorexia, thirst, and lumbago for the past four months. Since two months before admission, she had noticed chill, cough, and phlegm. She was markedly emaciated and pale. Her pulse was 100 per minute, regular, but somewhat weak, and body temperature was 35.9° C. Physical examination revealed hyperresonance and decreased breath sound accompanied by moist rales all over the lung. There was no palpable lymph node in the neck.

Roentgenographic examination revealed innumerable disseminated miliary densities all over the lung (Fig. 1). Glucosuria was negative, and albuminuria was of trace degree. No abnormalities were found in feces. Mycobacterium tuberculosis in sputum was negative on smear and culture. Erythrocyte sedimentation rate was 12 mm. per hour. Intracutaneous tuberculin reaction was negative.

She was given antituberculosis drug: paraaminosalicylic acid calcium, 10 gm.; isoniazid, 0.3 gm. per os; and streptomycin, 1 gm. intramuscularly daily. Toward evening on Feb. 4, she became somnolent, then became comatose on Feb. 11, and died on Feb. 13. The patient did not have a fever.

Pathological findings. The left pleura was adhered to the uppermost edge of the left lower pulmonary lobe. The left lung weighed 340 gm. and measured 19 × 12 × 4 cm.; the right lung weighed 450 gm. and measured 20 × 15 × 6 cm. They were red-violet and generally solid, but no induration was felt. There were innumerable miliary gray-white nodules in all cut faces. Microscopic examination revealed the proliferation of the relatively long spindle cells in the alveolar wall. The character of cylindric cells with nuclei in the basal region, lying in a line over the alveolar wall, is similar to those of bronchiolar carcinoma, with slight production of mucin substance (Fig. 2). There were a few normal alveoli. In spite of the absence of macroscopic swelling of the hilar lymph node, a few metastases were found therein microscopically. The liver weighed 860 gm. and measured 23 × 11 × 6 cm. Numerous miliary nodules were disseminated over the surface and the cut face and were microscopically of specific glandular structure of cubic tumor cells (metatasis on the liver). Liver cells were vacuolized and atrophic. Eminent hyperemia and slight infiltration of the small, round cells were found in the liver parenchyma. The kidney weighed 90 gm. (right) and



Fig. 1. Chest roentgenogram (Jan. 28, 1963)

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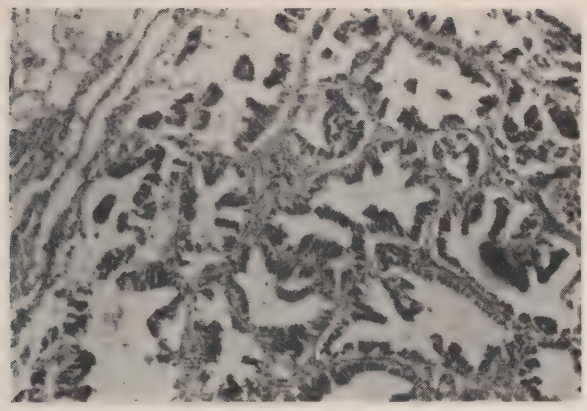


Fig. 2. Microscopic section of left lung

105 gm. (left), having a few miliary cysts over the surface and a few small, gray-white nodules that proved to be metastases on microscopic examination. There were no metastases in other organs. The thyroid gland showed no neoplastic nature.

DISCUSSION

In 1876 Malassez[1] reported the first case of this disease and was followed by Musser in 1903[2] and Helly in 1907.[3] This disease is considerably different from ordinary carcinoma of the lung, not only in the clinical picture but also in the pathological-histological findings. It is not yet decided which might be the origin of this tumor: the alveolar or the bronchiolar epithelium. Kagawa and associates[4] saw one case of this tumor of 109 patients with primary carcinoma of the lung, while the incidence of this tumor, according to other authors, is 1.5 to 5% of primary carcinoma of the lung. Our case is the only one of 32 with primary carcinoma of the lung for fifteen years in our clinic. Hematogenous metastasis of this tumor comes, in order, it is said, to the liver, abdominal lymph nodes, bone, adrenal gland, brain, kidneys, and so on. In our patient it was found in the hilar lymph node, the liver, and the kidneys.

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BASIC NEUROPHYSIOLOGIC ASPECTS OF EPILEPSY

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Environmental Teratogens and Birth Defects

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THE MAGNITUDE of the problem of the congenitally malformed child has been emphasized repeatedly during the past several years. An estimated 260,000 children were born in 1963 with some type of developmental defect. It is obvious that this is a most significant problem, not only to the afflicted child and his parents, but to the entire medical profession.

The basic understanding of the mechanisms involved in the causation of birth defects has been clarified to some extent in the past ten years by the outstanding discoveries made in the field of biochemical genetics. Paralleling this are the associated observations made by the cytogeneticist of the morphology of the human chromosomes. These significant advances have brought us to a point where it is possible that in the not too distant future the cause of many congenital anomalies may be better understood.

All of the research efforts being made in an attempt to discover the basic mechanisms involved in the production of birth defects have repeatedly demonstrated the need for a multidisciplinary approach to the broad problem of human teratology and the narrower problem of the effects of altered environment on the human fetus in utero. In addition to the laboratory research scientist, the obstetrician-gynecologist must actively participate in this field of investigation. He is the logical individual to clinically evaluate new drugs in the pregnant woman when they are ultimately approved for human use because of his special knowledge of embryology, his keen practical understanding of placental physiology, and his knowledge of the potentially harmful effects of drugs and infections on the fetus in utero.

The purpose of this review is to consider the hereditary, genetic, and environmental causes of developmental defects, and to speculate on the manner in which virus diseases might exert their teratogenic effect on the human embryo before birth.

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HEREDITARY DISEASES

The true hereditary diseases make up the majority of all genetically controlled afflictions. Everyone is familiar with the developmental defects inherited from generation to generation according to Mendel's genetic laws of segregation, independent assortment, and dominance and recessiveness. One of the most important and interesting advances made in this group in the past decade is the observation that specific enzyme deficiences can be inherited, resulting in metabolic alterations in the offspring which become evident in postnatal life. At the present time, approximately 52 of these so-called inborn errors of metabolism have been identified. One of these which is of considerable interest to the obstetrician and gynecologist is congenital virilizing adrenal hyperplasia which produces progressive virilization of offspring due to an enzymatic defect in the hydroxylation of hydrocortisone precursors.

CHROMOSOMAL ABERRATIONS

The second major teratologic mechanism which should be considered is the problem of chromosomal aberrations or "genetic accidents." Technical advances which occurred from 1952 to 1959 in the study of the cell nucleus made it possible to confirm the normal human chromosomal number as 46. It then rapidly became evident that many different types of human pathology were associated with a basic abnormality of either the number or morphology of the chromosomes. It also became evident that chromosomal aberrations could occur in either the sex chromosomes or the autosomes. For example, Turner's and Klinefelter's syndromes have a defect in the XY

group and monogolism, or Langdon Down's syndrome, is associated with an extra autosome in group 21-22 producing trisomy.

The basic cause of chromosomal aberrations is not entirely clear but the majority of these genetic accidents apparently occur during meiosis. Such mechanisms as nondisjunction, translocation, or deletion produce an excess or insufficient amount of nuclear chromatin in the resulting divided cells.

ENVIRONMENTAL EFFECTS

The third major cause of developmental defects are factors which affect the maternal-fetal environment and may interfere with orderly organogenesis, thereby producing developmental abnormalities. This is the area in which the obstetrician and gynecologist may play a most important role since the environment of the mother can be modified to some extent during pregnancy, provided she seeks prenatal care.

For convenience, the environmental factors currently known to produce malformations in man and similar mammals may be divided into 9 groups.

1. *Trauma.* The human embryo is protected in utero in such a fashion that it is extremely unlikely external trauma to the mother can produce developmental defects without causing fetal death or abortion. No absolutely proved cases of such traumatic malformations are on record, although from the medicolegal standpoint this may be the basis on which legal action is taken, especially following automobile accidents and other forms of personal injury. Unsuccessful attempts at instrumental abortion have been implicated as a cause of birth defects. If a child is born malformed following extensive intrauterine manipulations, the malformation is most likely the result of specific trauma to the fetus rather than a truly teratogenic effect on the developing child. The intrauterine amputation of limbs, which was thought at one time to be due to "amniotic bands" producing constriction and failure of development, has now been definitely shown to be the result of, and not the cause of, faulty development of the extremities.[1,2] Such bands represent an inferior quality or a primary focal deficiency of limb mesenchyme.

2. *Temperature changes.* Abnormal or rapidly changing temperatures may produce specific abnormalities in amphibia and occasionally in rats,[3] but the degree of temperature change required to produce similar anomalies in humans is probably not compatible with life. In addition, the temperature regulating mechanism of the human is reasonably effective and intrauterine temperature probably does not reach high enough levels to be teratogenic even in febrile illnesses of the mother. Abortion or malformations following maternal febrile infectious diseases are probably due more to a viremia or septicemia than to increased intrauterine temperature.

3. *Radiation.* It has long been recognized that X-irradiation can produce all manner of developmental defects in the human embryo when administered during the period of organogenesis.[4,5] After the first 3 months of gestation more subtile effects may be produced by X-ray and fetal disease or death may ensue if the dose is sufficient. This does not mean that all diagnostic X-ray studies should be precluded during pregnancy, especially when the fetus is near term and the exposure to the fetus is kept at an absolute minimum. The least amount of radiation needed to produce damage to the human fetus in utero has not been accurately determined. However, fetal malformations and abortion have been recorded following exposure to radiation of the degree required for barium enema, intravenous pyelography, gastrointestinal diagnostic studies, and fluoroscopy. Because of this, all women of the reproductive age group should be questioned as to the possibility of pregnancy before undertaking any diagnostic X-ray studies involving the abdomen or pelvis, and no purely elective abdominal examinations should ever be performed knowingly during the first trimester.

4. *Oxygen deficiency.* Hypoxia is a potent cause of developmental defects in experimental animals.[6,7] Mental deficiency and other central nervous system problems have been seen in human offspring following periods of maternal hypoxia resulting from carbon monoxide poisoning during pregnancy. The real problem of fetal oxygen deficiency is not so much that of its teratogenic action, but rather the long-term effect on the growth and development of the central nervous system after birth. Periods of hypoxia during labor and delivery certainly should be avoided if at all possible, and every attempt should be made to provide the fetus with an adequate oxygen supply at all times. The correction of maternal anemia during pregnancy, the rapid and effective treatment of placenta abruptio and placenta previa, and the early aggressive treatment of hypertensive states in pregnancy will substantially contribute to the welfare of the fetus by reducing the degree of fetal oxygen deprivation which may accompany any of these conditions.

5. *Nutritional disturbances.* In 1935, Hale[8,9]

produced anophthalmia and microphthalmia in pigs by feeding pregnant sows a vitamin A deficient diet. This study led the way to a large amount of experimental work which proved that maternal nutritional disturbances could produce various and predictable anomalies in the mammalian fetus. In addition to vitamin A, riboflavin, folic acid, and vitamin B_{12} deficiencies have been indited as causes of fetal malformations in experimental animals.[10,11,12] Whether nutritional and vitamin deficiencies are teratogenic in man is at present an unanswered question.[13] Since there are multiple interacting factors in the human diet, it is nearly impossible to identify or isolate a single specific dietary deficiency with accuracy. Long-term statistical studies of certain ethnic groups in which dietary restrictions are a mandatory part of their religious beliefs or extensive studies of offspring born during periods of famine would shed light on this problem. It is not likely, however, that faulty maternal nutrition plays a major teratogenic role in the human. Supporting this idea is the fact that in certain areas of the world where the majority of individuals subsist on minimal diets, the overall incidence of birth defects is not significantly different from those countries in which maternal nutrition is considered adequate.

6. *Hormonal disturbances.* It is now well established that hormonal imbalances of either maternal or fetal origin can produce developmental abnormalities in the offspring. Hyperplasia of the fetal adrenal cortex is known to cause pseudohermaphroditism of the female fetus or macrogenitosomia praecox in the male. Congenital cretinism is another example of intrinsic fetal hormonal disturbance affecting intrauterine growth and development.

At the present time, an important problem to the physician is the potential teratogenic effect of synthetic progestational agents on the external genitalia of the female fetus when these drugs are administered to the mother during pregnancy. Many synthetic progestins are quite similar to testosterone both chemically and pharmacologically. When given in fairly large doses early in gestation and continued for several months, masculinization of the female external genitalia can occur.[14] Again, this does not mean progestational agents, both synthetic and natural, should not be used in pregnancy when indicated. This observation serves to reemphasize the importance of keeping the dose of any drug and duration of treatment at a minimum therapeutic level during pregnancy.

7. *Miscellaneous environmental factors.* A number of statistical investigations have been undertaken over the years in an attempt to correlate human developmental defects with such various factors as the season of the year in which conception occurred, locality of birth, population density, and climate. Obviously, any such study is affected by many variables and is extremely difficult to interpret. There is, however, statistical evidence that the risk of congenital anomalies such as achondroplasia, anencephaly, hydrocephaly, and other gross malformations of the central nervous system increases with maternal age. In addition, about 40% of mongoloid infants are born of mothers over 40 years of age.[15–17] In view of this, the physician may do his patient a service by encouraging her to complete her family by the age of 38 or 40. This suggestion would probably be most agreeable to the majority of women.

8. *Drugs and medications.* All drugs used by man, if given in sufficient amounts, are poisons. Many medications in daily use which are commonly considered to be harmless, such as nicotine, caffeine, and aspirin, are teratogenic and produce specific predictable fetal abnormalities when administered at the proper time of gestation to specific animals in adequate dosage.[18–20] In theory then, no pregnant woman should receive any drug of any kind during gestation. This is obviously an impractical suggestion. To withhold a necessary drug from a pregnant woman simply on the basis that it might possibly affect the fetus adversely would be injudicious. If this policy were followed, the fetal and maternal morbidity and mortality from the specific disease being treated would far outweigh the beneficial effect to the occasional fetus which would be spared. A reasonable and thoughtful approach to drug therapy in the pregnant individual must be practiced until the teratogenic risk of all drugs has been established and the mechanism of their action is fully understood. It would seem logical to suggest that the physician continue to administer to his pregnant patient, when necessary, drugs which have been proved by long use to have no apparent adverse effect on the fetus when given in the usual and recommended dose. The indiscriminate administration during pregnancy of many combinations of drugs or the use of medications of unproved toxicity is unwise because of the potential risk to the developing fetus, even though slight.

9. *Infections.* During the past several decades, it has become apparent that the fetus in utero is succeptible to many types of bacterial and viral infections. The virus of rubella has an especially

potent teratogenic effect when the fetus is exposed during the period of organogenesis. It has been estimated that between 17 and 50% of offspring will have major congenital defects when maternal rubella occurs in the first three months of pregnancy.[21,22] Many other virus diseases have little or no effect on the developing infant and the reason for the particularly damaging effect of the rubella virus is not yet known. Certain other conditions such as toxoplasmosis and cytomegalic inclusions disease may affect the fetus and produce hydrocephalus, microphthalmia, and other abnormalities recognizable at birth. This latter situation almost always represents the results of intrauterine disease in the normally developed fetus and not a true teratogenic effect of the infecting organism. Since no adequate drug therapy against virus infections exists at the present time, the physician should attempt to provide his patient with proper protective immunization against any infectious disease to which the mother has not had an opportunity to develop a natural immunity.

The exact mechanism by which virus exerts its teratogenic effect is presently unknown. On the other hand, reasonable evidence exists that some biochemical interference with deoxyribonucleic acid (DNA) metabolism occurs when a cell becomes parasitized by virus causing the cell to become chemically abnormal.

It is now believed that a chromosome consists of a long chain of DNA molecules that are twined around each other to form a helix, and that genes are segments of this chain. The DNA molecule is made up of 2 sugar-phosphate groups that are linked together by the nitrogenous bases, adenine, thymine, guanine, and cytosine, forming a nucleotide. Adenine and guanine are purines, and thymine and cytosine are pyrimidines.

The sequential arrangement of these nucleotides in the DNA helix is thought to determine the genetic information transmitted during cellular reproduction. Alteration or interruption of this arrangement could transmit erroneous or inadequate information to the new cell and perhaps result in failure of production of an essential enzyme or amino acid. This abnormal cell then might continue to reproduce and as a result, malformation of the developing organ or tissue could occur.

Since viruses are intracellular parasites and usually reproduce in the nucleus adjacent to the nuclear chromatin material and since many viruses contain large amounts of DNA, it seems reasonable that virus DNA could interfere in some way with the DNA of the normal cell resulting in an abnormal genetic code. Thus virus might exert its teratogenic effect in one of the following ways:

1. Intramolecular interferences with DNA replication could occur by the substitution of a viral nucleotide for a cell nucleotide in the DNA molecular sequence. This would cause erroneous metabolic information to be transmitted to the next reproducing cell.

2. Viral DNA could, without inducing pathologic change, combine with the chromosome system of the infected cell in the manner of a transmittable gene. This might possibly interfere with the uncoiling of the DNA helix, thereby preventing complete replication of that chain.

3. Several investigators have shown that following certain virus infections there is an increased synthesis of DNA accompanied by an increased utilization of glucose.[23,24] With increased glycolysis there is a resulting accumulation of organic acids in the infected cell resulting in a marked pH change to acid. Perhaps an intense intracellular metabolic change such as this could interfere with normal cellular reproduction.

CONCLUSION

Any attempt to summarize all of the factors which might possibly contribute to the defective development of the fetus must by necessity be incomplete, since our present knowledge of these factors is so fragmentary. Despite a lack of complete understanding of these problems, the practicing physician is in a position to help modify and occasionally prevent the occurrence of events during pregnancy which might affect the fetus adversely. By doing so, the number of children born with developmental defects may be decreased significantly.

Read before the 26th Annual Meeting of the North Dakota Society of Obstetrics and Gynecology, Fargo, North Dakota, September 12, 1964.

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SALMONELLOSIS has not been eradicated by antibiotic therapy and may even be increasing. Postoperative infections appearing as simple bacteremia, overwhelming septicemia, an unusual form of focal infection, or localized abscess formation may pose special problems, particularly in debilitated elderly patients and those with underlying systemic disease. Altered postoperative physiology may activate a latent infection, surgical manipulation of the gastrointestinal tract may spread infection, or preoperative antibiotics may alter the gastrointestinal bacteria. Diagnostic problems in salmonellosis include fever of undetermined origin, acute and chronic enterocolitis, and obscure complications.

Treatment of salmonellosis varies widely with different manifestations, and the only definitely established therapy is chloramphenicol for typhoid fever. Cholecystectomy is recommended if a two-week course of antibiotics does not eradicate the organism or if patients have gallstones. Both pre- and postoperative medication should be given. Such supportive measures as maintenance of fluid and electrolyte balance may be adequate treatment for enteric infections, but kanamycin and ampicillin should also be given to prevent future systemic or focal salmonella infection. Tetracycline and streptomycin are given for any bacteremia due to gram-negative organisms but, if the patient is not recovering when the organism is identified as salmonella, ampicillin or kanamycin is substituted. Massive doses of oral penicillin combined with probenecid, furazolidone, polymyxin B, and neomycin may be tried for resistant infections. Focal infections are treated by surgical incision and drainage. Over a period of fifteen years, 94 salmonella infections have been seen, 21 asymptomatic, 46 enteric, 16 in the bloodstream, and 11 focal. The infection was first detected after operation in 13 patients.

RONALD A. COHEN, M.D., JOSEPH E. GERACI, M.D., WILLIAM H. DEARING, M.D., and GERALD M. NEEDHAM, PH.D., Mayo Clinic and Foundation, Rochester, Minn. Salmonellosis: Observations on 94 patients. Mayo Clin. Proc. 39:401-409, 1964.

Malignant Mesenchymoma of the Heart

Report of a Case

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CARDIAC TUMORS are uncommon and few are diagnosed before death. The malignant neoplasm which is the subject of this report is particularly uncommon, only one other such tumor having been described previously.

CASE REPORT

A 26-year-old Filipina woman entered the hospital in October 1961, with a history of easy fatigability, shortness of breath, and vague chest pains beginning three years before and becoming increasingly severe in the previous three months. Examination of the chest revealed absent breath sounds in the right lower chest. The blood pressure was 100/60 mm. Hg. The pulse was 106 per minute. There were no murmurs, but P_2 was louder than A_2. A chest roentgenogram showed a convex left heart border, and a repeat film ten days later showed fluid in the right lower chest (Fig. 1). A lateral view showed encroachment upon the retrosternal space by the right ventricle. There was a suggestive enlargement in the region of the left atrium. Mild hemoptysis was noted in December 1961.

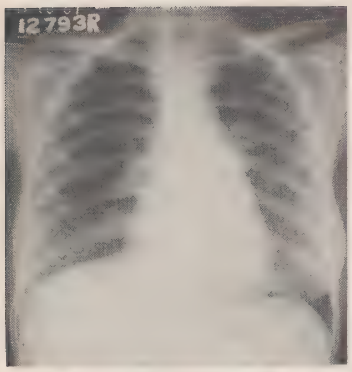
In January 1962, she developed left scapular pain radiating to the precordium. Minimal pedal edema now appeared. Her ECG (Fig. 2) showed diphasic P waves in leads 1, AVL, and V1; a wide negative component in V1 and notched in V3-5; a P-R interval of 0.11 seconds; a Q-R-S interval of 0.06 seconds; inverted T waves in 3, AFV, and V1-4. The pedal edema disappeared after oral thiazide therapy only to recur in the latter part of April 1962. She now complained of sharp right lateral chest pain which was worse when she was recumbent. The arm-to-tongue circulation time was now fourteen seconds. ECG now showed incomplete right bundle branch block and cor pumonale. In May 1962, eight months after hospitalization, she developed a thrill just to the left of the sternum and a loud systolic murmur appeared for the first time. This was heard just to the left of the sternum and disappeared precipitously near the apex. The murmur did not radiate.

The patient died in October 1962. The last five months of life were marked by steady deterioration of her physical status. She developed a tender pulsating liver, bounding jugular veins, and pedal edema resistant to diuretic therapy. One month before death the systolic murmur acquired a musical quality which disappeared when she took a deep breath. A chest film taken at this time (Fig. 3) serves to show the amount of cardiac enlargement which had occurred in the previous ten months.

Necropsy findings. There was pitting edema of the skin of the lower extremities and of the trunk to the level of the umbilicus. The pleural, pericardial, and peritoneal cavities were filled with clear fluid. The liver edge was at the level of the anterior-superior iliac spine.

Heart. The heart weighed 434 gm. The epicardium was smooth and there were petechiae in the left atrioventricular sulcus. The outer surface of the left atrium bulged outwards and the atrium was unusually firm (Fig. 4). The left pulmonary veins were patent. The walls of the right pulmonary veins were eccentrically thickened by firm white tissue, causing marked narrowing of their lumens. The lumen of the right superior vein was slit-like and the lining surface of this vessel was covered by a thin film of friable blood clot. The lumen of the right inferior pulmonary vein, just before entering the heart, was occluded by a firmly fixed thrombus. The chamber of the

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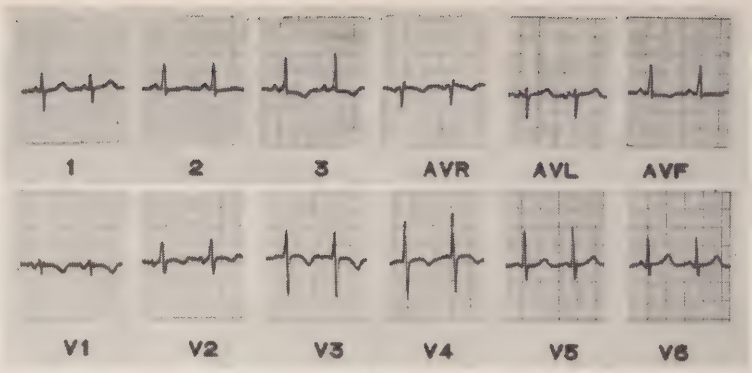


Fig. 1. *(Left)* Chest film showing convex left heart border. Fig. 2. *(Right)* Electrocardiogram, January 1962

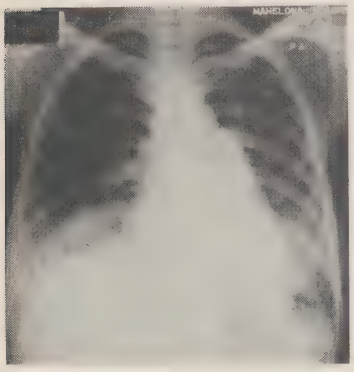


Fig. 3. Chest film showing progressive enlargement of heart shadow

left atrium was narrowed to a slit by a mass in its wall. The mass involved the septal, superior, and posterior aspects. The wall measured up to 2 cm. in thickness in these areas and was yellowish white in appearance. A 4 cm. × 6 cm. cylindrical projection from the septal aspects of the mass further narrowed the lumen. This extended downwards, overlying the posterior leaflet of the mitral valve (Fig. 5). The cut surface of this downward projection had a cartilagenous consistency. The chamber of the left atrial appendage was not dilated and contained thrombus which was easily removed. The wall of the appendage was not involved by tumor.

The mitral and aortic leaflets were thin and delicate. The left ventricular wall showed no gross changes and measured 1.2 cm. in thickness. The coronary ostia were widely patent. The chambers of the right heart were smooth. The pulmonary and tricuspid valves were thin. The pulmonary ring measured 7 cm. in circumference, and the tricuspid ring was 11 cm. The right ventricle measured 2 mm. in thickness.

Microscopic examination of the left atrial mass revealed it to vary greatly in appearance from area to area. The mass projecting

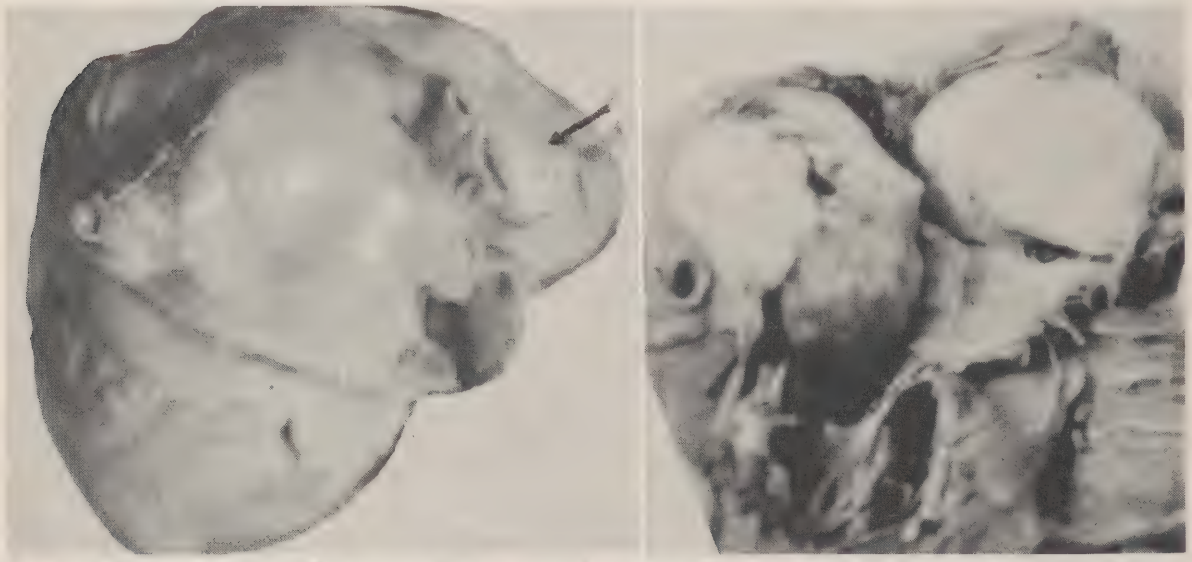


Fig. 4. *(Left)* External view of left atrium. Note outward bulge caused by intramural mass and the extension of tumor into right inferior pulmonary vein (arrow). Fig. 5. *(Right)* Opened left heart showing atrial mass. The rounded mass projecting into lumen was found to be composed almost entirely of chondroblastic tissue.

into the lumen was found to be composed largely of pleomorphic chondroblastic elements (Fig. 6). Small chondroblastic foci were seen in other areas as well, but nowhere else did they constitute the bulk of the tumor tissue. Sections of other portions of the neoplasm revealed osteoblastic (Fig. 7), fibroblastic (Fig. 8), lipoblastic, and rhabdomyoblastic areas (Fig. 9). Cytoplasmic cross striations were readily apparent in the last. Still other zones resembled primitive vascular tissue. No epithelial elements were identified in the mass. The grossly unaffected endocardium of the left atrial appendage and the intima of the unaffected portions of the pulmonary veins were lined by a layer of thick connective tissue. These tissues contained occasional plump, hyperchromatic, spindle-shaped nuclei.

Lungs. The left lung measured 460 gm., the right, 350 gm. The lungs were poorly aerated and had a meaty consistency. The upper lobe of the right lung contained a wedge-shaped, 3 cm., dark red, nonaerated zone. The pulmonary artery serving this area was filled with firmly attached thrombus. The cut surfaces of the lungs varied from dark red to reddish-brown, the former appearance predominating in the basal aspects.

Microscopic examination showed an infarct in the right upper lobe and revealed intense congestion of the septal capillaries elsewhere. The alveolar spaces were filled with red cells and hemosiderin-laden histiocytes. The pulmonary arteries were thin-walled. Some alveoli contained sufficient neutrophils and fibrin to merit the diagnosis of bronchopneumonia.

Liver. The liver weighed 1,228 gm. and had accentuated vascular markings. Histologic examination revealed great dilation of the central veins and hepatic sinusoids. This was associated with central necrosis of the lobules.

Adrenal glands. The adrenal glands were not unusual grossly, but microscopic examination showed a pronounced increase in the amount of connective tissue in the medulla, to the extent that it was difficult to find chromaffin tissue. This connective tissue was acellular and densely collagenous in type. It enclosed many capillaries and venules plugged with calcific material. The cortex was somewhat thinner than usual but all three layers were readily identified.

Gross and microscopic examination of the gastrointestinal tract, thyroid gland, bone marrow, lymph nodes, kidneys, spleen, pancreas, uterus, ovaries, and central nervous system yielded no significant pathologic changes.

Summary of anatomic findings. There was a malignant tumor of the left atrium of the heart composed of bizarre forms of many mesenchymal tissue types. There was intense congestion of the lungs, complicated by bronchopneumonia and infarction, and of the liver with central necrosis of the lobules. There was an incidental medullary fibrosis in the adrenal glands, associated with calcific plugs in the medullary veins and capillaries. It is felt that these were most likely calcified thrombi.

DISCUSSION

Hagstrom[1] noted that only 135 primary malignant tumors of the heart had been reported up to 1960. He reported a case of malignant mesenchymoma arising from the region of the pulmonary artery, which he believed to be the first tumor of its kind in this situation. Coe's[2] review of cardiac sarcomas listed 149 of these tumors, none similar to that seen by Hagstrom or described in our report. Review of published reports of malignant mesenchymoma fails to establish any, other than Hagstrom's, arising in the heart. As defined by Stout,[3,5,6] who first described this tumor, the neoplasm must contain 2 or more malignant mesenchymal elements not ordinarly associated together. He has pointed out that since most tumors of mesenchymal derivation have fibrosarcomatous areas, this form is not recognized as a separate one in evaluating tumors. He also noted that the presence of adult, differentiated bone or cartilage in a tumor such as a liposarcoma does not indicate that it is another malignant element. Each mesenchymal element of the tumor must be a malignant one. The neoplasm in our patient meets these criteria.

The question might be raised as to whether this tumor is not a malignant teratoma. Teratomas have been reported in the heart, and are composed of diverse tissue elements. There are, however, good reasons for believing that the tumor in our patient was not a teratoma. There were no ectodermal, endodermal, or neural elements in this tumor, and no adult tissues of any type. Willis[4] has pointed out that a mixture of differentiating elements of all ages is one of the most striking features of actively growing teratomas. This view appears substantiated in William's recent review of cardiac teratomas.[7] He noted that, up to 1961, there have been 14 reports of benign intrapericardial teratomas. The tumors characteristically form a pedunculated mass at the base of the great vessels and only one had penetrated the myocardium. All 3 germ layers were found in 11 of these patients, but only respiratory tissues in the only other patient reported in histological detail. The only malignant

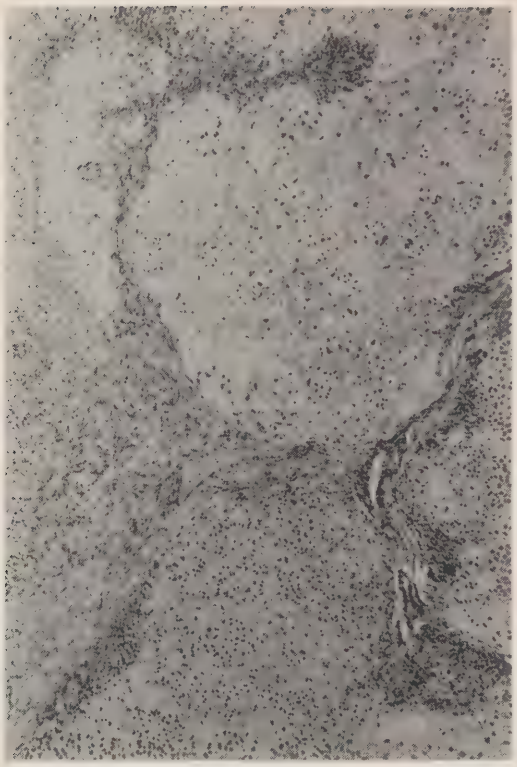


Fig. 6. Photomicrograph showing chondroblastic area (× 45)

Fig. 7. Photomicrograph showing osteoblastic area (× 400)

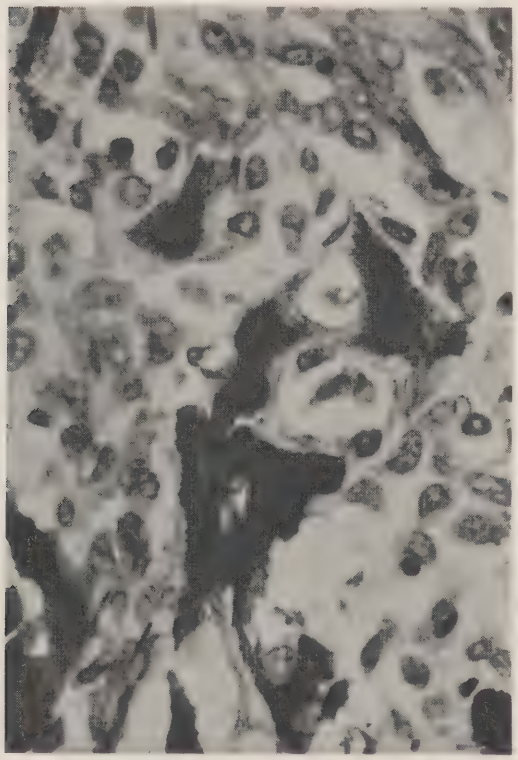


Fig. 8. Photomicrograph showing fibroblastic area (× 400)



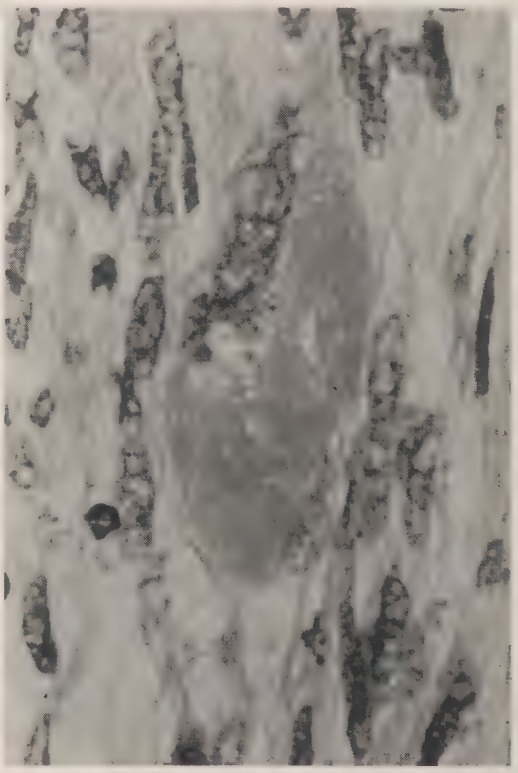


Fig. 9. Photomicrograph showing strap cell with cross striations in rhabdomyoblastic area (× 500)

teratoma of the heart is that of Solomon.[8] This tumor, occurring in a 2-year-old girl, arose from the interatrial septum and extended into the right atrium. This tumor contained well differentiated cells having the appearance of epithelium. No carcinomatous component was identified. In summary, therefore, the tumor is probably not teratomatous because it does not have the characteristics of malignant teratomas arising at other sites; because cardiac teratomas usually arise in the pericardium, rather than within the heart substance; because benign cardiac teratomas usually contain all three germ layers; and because the only malignant teratoma reported to date contained both adult and undifferentiated epithelial elements, but no sarcomatous tissues.

In Stout's original description of mesenchymoma,[5] he stated that it is a dysontogenetic growth. He also noted that the mesenchyme is an extremely versatile tissue, which, in orderly development, produces the normal prototypes of all the tissues of which these cells are caricatures. At the same time he showed that this tumor did not always arise in regions showing a predilection for congenital malformation, and his subsequent papers confirm this observation. Although cardiac tumors are not especially common, it would seem likely that, in proportion to mass, the heart is at least as common a source of mesenchymal tumors as the soft tissue which cloaks the skeleton. All mesenchymal elements, except bone and cartilage, commonly share in the production of these cardiac tumors. There is no apparent association between mesenchymal neoplasms and cardiac anomalies. The occurrence of malignant mesenchymomas in the heart serves to emphasize the fact that mesenchymal elements at this site are no less versatile than those in soft tissues.

It should be noted that neither Hagstrom's patient nor ours showed any evidence of metastatic disease. This suggests that this tumor is slow growing and relatively nonaggressive, since each patient had symptoms at least four years prior to death. It also suggests that discovery of the tumor by cardioangiography, early in the course of her disease when mild symptoms first appeared, might have permitted successful surgical removal. Nash and Stout[3] have shown that survival with soft tissue tumors of this type is related to the size of the tumor. Nine out of 14 of their patients were without recurrence when the tumor measured less than 5 cm. in diameter.

SUMMARY

Necropsy of a young woman who died of heart failure showed that this was caused by a malignant mesenchymoma arising in the wall of the left atrium of the heart. This is the second such tumor to be reported. Both recorded tumors caused symptoms years prior to death and neither tumor had metastasized. They resembled, both in structure and behavior, similar tumors occurring in the soft tissue.

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SPIDER NEVI occur in 22% of boys and 30% of girls age 15 or younger, most often on dorsum of hands and forearms, with the largest nevi usually on the face. The lesion is insignificant in healthy children, and incidence does not increase in children with chronic illness or congenital abnormalities. Incidence does increase to 39.5%, however, in children with diseases of the central nervous system. In the total population, incidence increases rapidly after 2 years of age, levels at puberty, and decreases to 10 to 15% in adults. Studies were done of 220 children with chronic illnesses, 86 with central nervous system disease, and 407 healthy controls.

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Pediatrics 33:227-232, 1964.



Philip Showalter Hench, M.D.

JAMES ECKMAN, Ph.D.
Rochester, Minnesota

DR. PHILIP SHOWALTER HENCH, a member of the staff of the Mayo Clinic from 1923 to 1957, world-famous authority on arthritis, pioneer in the clinical use of cortisone, and co-winner of the Nobel Prize in physiology and medicine in 1950 for his work with that hormone, died at Ocho Rios, Jamaica, on March 30, 1965, of pneumonia and diabetic coma.

Dr. and Mrs. Hench had gone to Jamaica for a vacation on March 21. Their son, John B. Hench, a student at Lafayette College, Easton, Pennsylvania, had joined them there for the spring vacation at his school.

Dr. Hench was born in Pittsburgh, Pennsylvania, on February 28, 1896, the son of Jacob Bixler Hench and Clara John Showalter Hench. His father, J. B. Hench, Litt. D., was a scholar of the classics, a well-known preparatory-school teacher, and an educational leader in western Pennsylvania.

Dr. Hench received his preparatory-school education at the Shadyside Academy and at the University School, both of Pittsburgh. He was granted the degree of bachelor of arts from Lafayette College, Easton, Pennsylvania, in 1916, and the degree of doctor of medicine from the University of Pittsburgh in 1920. After a year's internship at Saint Francis Hospital in Pittsburgh he became, in October 1921, a fellow in medicine in the Mayo Graduate School of Medicine of the University of Minnesota. In 1923 he became a first assistant and a member of the staff of the Mayo Clinic. He was appointed an associate in 1925, and in 1926 became a consultant in the division of medicine and head of the new section on rheumatic diseases of the Mayo Clinic. In 1953 he became a senior consultant of the Mayo Clinic, and he retired from the Mayo Clinic and Mayo Graduate School of Medicine on July 1, 1957.

Dr. Hench studied abroad between October 1928, and May 1929, being chiefly with Dr. Ludwig Aschoff at the University of Freiburg, Germany, and with Friedrich Von Müller at the Ludwig-Maximilians-Universität, Munich.

He was married on July 14, 1927, to Mary Genevieve Kahler, daughter of John Henry Kahler, of Rochester who, at the request of Dr. W. J. Mayo and Dr. C. H. Mayo, had developed for the use of the staff of the Mayo Clinic and its patients the Kahler Corporation's group of hospitals, hotels, and supporting institutions. Dr. and Mrs. Hench have 4 children: Mary Showalter, now Mrs. John B. Henty, of Ormond Beach, Florida; Dr. Philip Kahler, of La Jolla, California; Susan Kahler, now Mrs. Frederick Bowis, of Bethesda, Maryland; and John Bixler, a student at Lafayette College.

In the Mayo Graduate School of Medicine, University of Minnesota at Rochester, Dr. Hench was instructor from 1928 to 1932, assistant professor from 1932 to 1935, and associate professor from 1935 to 1947. From 1947 to 1957 he was a

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full professor of medicine in the Mayo Graduate School of Medicine.

While a medical student during World War I, Dr. Hench enlisted in 1917 as a private in the medical corps of the Army of the United States, but he and his classmates were transferred to the enlisted reserve corps to finish their medical training. In World War II, Dr. Hench entered military service in August 1942, as lieutenant colonel in the medical corps, Army of the United States, serving first as chief of the medical service at Camp Carson, Colorado, and then as chief of the medical service and director of the Army's rheumatism center at the Army and Navy General Hospital. He was promoted to the grade of colonel in 1945. After being inactivated, in January 1946, he became an expert civilian consultant to the surgeon general, United States Army.

In 1931 he received the degree of master of science in internal medicine from the University of Minnesota. He was awarded the honorary degree of doctor of science by Lafayette College in 1940, Washington University and Jefferson College in 1940, Western Reserve University in 1950, the National University of Ireland in 1950, the University of Pittsburgh in 1951, Gustavus Adolphus College in 1963, and the honorary degree of doctor of laws from Middlebury College in 1951.

For many years Dr. Hench was considered one of the leaders in American rheumatology, being one of the founders of the American Rheumatism Association, of which he was president in 1940 and 1941. As the culmination of many years of clinical studies in the treatment of rheumatoid arthritis, Dr. Hench, in 1948, introduced into clinical medicine the steroid hormone, cortisone, developed after a long period of laboratory investigation by Dr. Edward C. Kendall, of the Mayo Clinic. The 2 men had worked together incessantly on the problem, one from the clinical viewpoint and the other from the biochemical and physiological aspects. In 1950 Dr. Hench and Dr. Kendall, with Dr. Tadeus Reichstein, of Switzerland, were awarded the Nobel Prize in physiology and medicine "for discoveries in the hormones of the adrenal cortex, their structure and biological effects."

Additional honors were accorded Dr. Hench and Dr. Kendall. Jointly they received the 1949 Lasker Award, presented in 1950 by the American Public Health Association; the 1950 Page-One Award of the New York chapter of the American Newspaper Guild; the 1950 Passano Foundation Award; the 1950 Scientific Award of the American Pharmaceutical Manufacturers' Association, with Professor George Thorn of Harvard University; the Award of Merit of the Masonic Foundation for Medical Research and Human Welfare in 1951; Northwestern University Centennial Award in 1951; special citation from the Regents of the University of Minnesota in 1951; and the 1951 Dr. C. C. Criss Award "for the greatest contribution to public health during the year 1950." In 1954 Dr. Hench and Dr. Kendall were recipients of the distinguished service award for alumni of the Sigma Alpha Epsilon academic fraternity.

Dr. Hench was awarded the Heberden Medal in London in 1942, a special citation of the American Rheumatism Association in 1951, and a special citation from the board of managers of the Walter Reed Memorial Association in 1953. He was also the recipient of the 1951 "Pennsylvania Ambassador" Award from the Pennsylvania State Chamber of Commerce "for outstanding achievement in the best traditions of the Commonwealth." He was given the award of honor of the Mississippi Valley Medical Society for 1952. On January 25, 1952, he was invested with the Order of Carlos J. Finlay by the Republic of Cuba, and on October 10, 1953, with the Orden Nacional de Merito, Carlos Manuel de Cespedes, also by the Republic of Cuba. He was 1 of 7 distinguished guests at the annual meeting of the American College of Physicians in Minneapolis in 1956. In 1958 his associates and former students at the Mayo Clinic and Mayo Foundation established the Philip Showalter Hench Scholarship Fund in his honor. In the same year he received the *Modern Medicine* award for distinguished achievement in the clinical application of the hormones of the adrenal cortex to the treatment of rheumatoid arthritis. That year the Women's Auxiliary of Pittsburgh gave him special honors in connection with the Pennsylvania Bicentennial, and Northwestern University presented him with a special citation "in recognition of his outstanding contributions to the knowledge of the metabolic aspects of rheumatology and collagen diseases and for exceptional meritorius achievement in pioneering the experimental and clinical use of cortisone in the relief of rheumatic diseases."

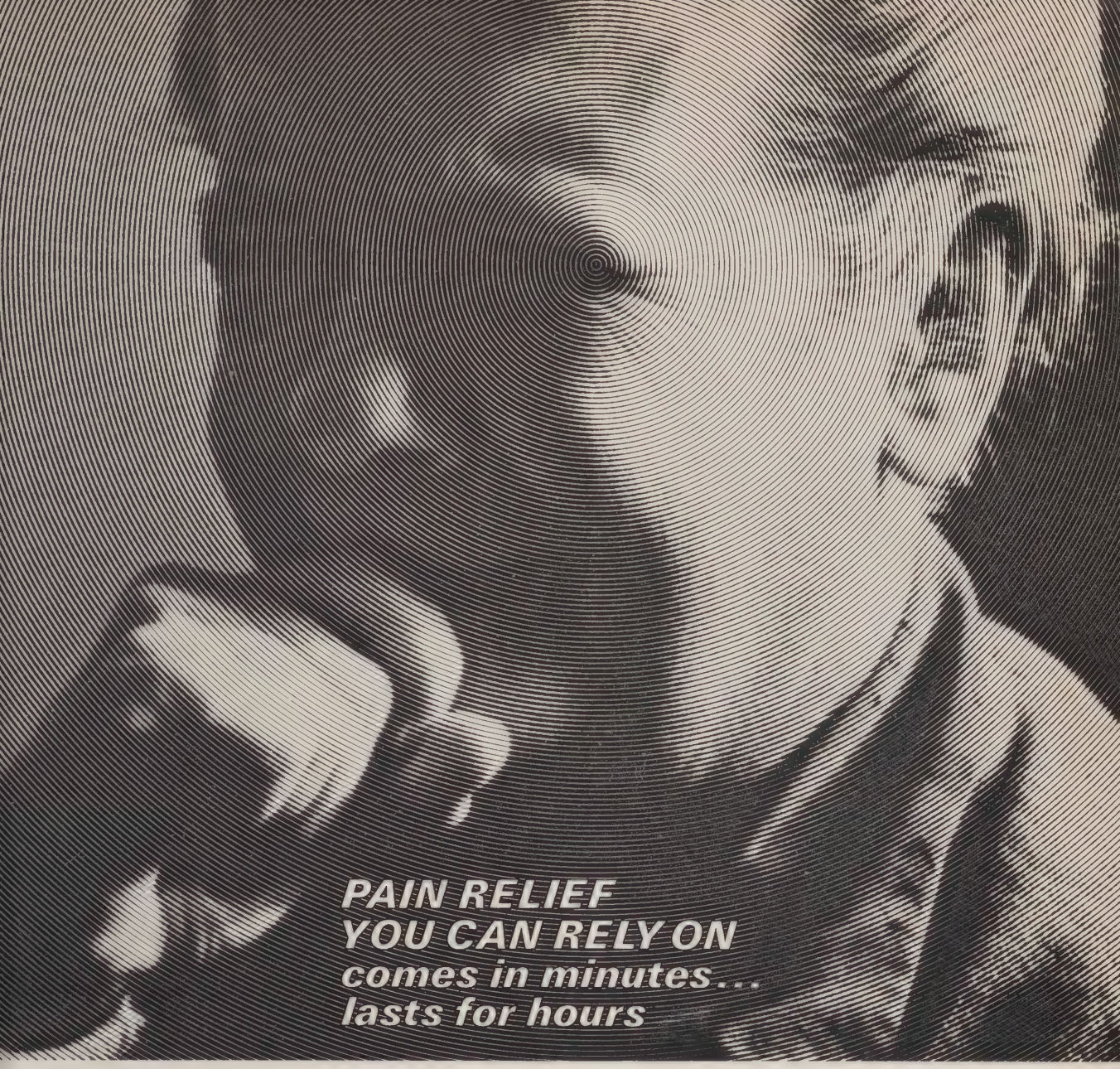
At a New York Academy of Sciences dinner and reception in December 1958, Dr. Hench, with Dr. Kendall, was honored on the occasion of the first decade after the discovery of the therapeutic usefulness of cortisone. In 1960 he was given the award of the American College of Physicians. In 1961 he was one of 10 Nobel Prize laureates honored by the American Association of Land Grant Colleges and State Universities, and on April 29, 1962, with Mrs. Hench,

he was among the 49 winners of a Nobel Prize honored by President John F. Kennedy at a reception and dinner at the White House.

Dr. Hench from 1932 to 1948 was the chief editor of the American Rheumatism Association's annual *Rheumatism Reviews* and he had been associate editor of the *Annals of Rheumatic Diseases* (London). He also had been chairman of the American Committee of the Ligue Internationale contre le Rheumatisme. He was chairman of the Arthritis and Rheumatism Study Section of the National Institutes of Health, United States Public Health Service in 1949 and 1950, and was a member of the Advisory Council of the National Institute of Arthritis and Metabolic Diseases, United States Public Health Service. He also was titulate to the Central Committee of the Pan-American League Against Rheumatism, a member of the Advisory Committee of the National Research Council, and a member of the Medical and Scientific Committee of the Arthritis and Rheumatism Foundation. In 1962 he was appointed a member of the Commission on Drug Safety for advancement of the predictability of the action of new pharmaceuticals in the human being.

Dr. Hench was an honorary member of the American Academy of Arts and Sciences; the Royal Society of Medicine, London; the Royal Academy of Medicine of Belgium; the Heberden Society, London; the Liga Argentina contra el Reumatismo, Buenos Aires; Mississippi Valley Medical Society; Swiss Society of Physical Medicine and Rheumatology; Société Medicale d'Aix-les-Bains; Liga Brasileira contra o Reumatismo; Canadian Rheumatism Association; Danish Rheumatism Society; the Ligue Française contre le Rheumatisme; the Sociedad Española de Reumatismo; Svensk Rheumatologisk Forening; and the Swedish Medical Society. Other memberships include the Association of American Physicians, Associacao Portuguesa de Reumatologia, American Society for Clinical Investigation, Central Society for Clinical Research, Minnesota Society of Internal Medicine, and Association of Military Surgeons of the United States and he also was a Regent of the American College of Physicians. He was an honorary corresponding member of the Sociedad Cubana de Salubridad Pública. He was vice-president of the Board of Managers of the Walter Reed Memorial Association of Washington, D.C., and was vice-president of the Kahler Corporation of Rochester, Minnesota, from 1951 to 1963. He was a member of the Alpha Omega Alpha medical honor society, Sigma Alpha Epsilon academic fraternity, the Sherlock Holmes Society of London, Norwegian Explorers' Club of Minneapolis, the Society of the Sigma Xi, Nu Sigma Nu professional medical fraternity, and an honorary member of Phi Beta Kappa, honorary academic scholastic fraternity.

His hobbies were tennis, music, photography, and the writings of Sir Arthur Conan Doyle. He published original investigations on medical history, being considered an authority on the conquest of yellow fever. In 1958 he contributed an essay on "Of Violence at Meiringen," describing the escape of Sherlock Holmes in 1891 from death at the hands of Professor Moriarty at the Reichenbach Falls, and telling how Hench and others combined to put up a plaque on the spot in 1957 to mark the scene of the incident. This essay was printed in the volume, *Exploring Sherlock Holmes*, issued in 1958 by the Norwegian Explorers' Club of Minneapolis.



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Book Reviews . . .

Dynamic Pathology—Structural and Functional Mechanisms of Disease

by MAURICE M. BLACK *and* BERNARD M. WAGNER, *296 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1964. $8*

This is an excellent text. The authors successfully correlate the physical state with disease states. The function of the elements with the normal cell is well presented. The homeostatic functions of the normal cell and the occurring abnormalities in circulatory or organ disease states give one a better understanding of the mechanisms of diseases.

The normal metabolism of the cell and the function of cell particles such as the mitochondria, Golgi's apparatus, endoplasmic reticulum, and nucleus are described. There are chapters on genetics, development, and the vascular system, with a good discussion on blood clotting.

DONALD AMATUZIO, M.D.
Minneapolis

Common Complaints: Consultations in Medicine

a collection of medical articles from CONSULTANT *magazine, 206 pp., ill., Smith, Kline & French Laboratories, Philadelphia, 1964. $3*

This is a book written by many experts. It can be of great value to any physician, and doubtless many will be glad to have it on the shelf back of their desks. The articles are well written and, in a couple of pages or so, can supply much valuable information which can be very useful to a physician. For instance, on page 128, there is a brief article on acne by Frances M. Keddie, M.D., and Thomas H. Sternberg, M.D. They have been getting good results, not in ordinary acne but in cases of cystic and scarring acne, by using triamcinolone and dexamethasone. As soon as the doctors see good improvement, they start decreasing the dose of the drug. At first they used an antibiotic in conjunction with the steroids but later found it was unnecessary except in rare instances. They say that ordinarily, control of this type of acne can be maintained with corticosteroids until such time as the acne wears itself out and spontaneously disappears. The authors don't know just why the corticosteroids work so well in cases of acne.

They say, however, that, "We have not tried this treatment for juvenile or ordinary pustular acne, nor do we advise it. What it does is to provide a method for preventing the severe scarring associated with deep pustular acne. In the experience of the contributors, the prolonged use of corticosteroids in young people, with proper medical control, has not been accompanied by serious side-effects." In some cases, the disease can be controlled with a strong antibiotic such as tetracycline.

The authors no longer use X-rays in the treatment of acne. Some dermatologists have quit using irradiation, largely because of the danger of damage suits. Some feel that in cases of acne, iodized salt should not be used.

An interesting chapter (p. 111) by Dr. Garrard is on some psychic disturbances that call for treatment, not only of the patient but of his family. This is one of the big problems of many a physician today. It would be a wonderful thing if all physicians could read the excellent

(Continued on page 16A)

when treatment might precipitate a problem with monilia

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(Continued from page 14A)

chapter on pathological depression, written by Dr. James R. Harris. As Dr. Ayd has said so well, today the commonest mistake in diagnosis met within doctors' offices is to fail to recognize a depression. Too often the doctor becomes concerned only over the patient's stomachache or miserable feeling in some part of the body.

WALTER C. ALVAREZ, M.D.
Chicago

Atlas of Blood Cytology

by G. FORTEZA BOVER, *511 pp., ill., Grune & Stratton, Inc., New York City, 1964. $39.50*

This is a most interesting atlas. The authors use the first part of the book to discuss the staining methods used in differentiating various cells. Also discussed are the cytochemical stains used for distinguishing nucleic acids, various metals, and enzymes and fluorescent microscopy techniques with acridine orange dyes for RNA and DNA and chromosome analysis. By looking into the first part of this book, one should be able to produce some of the fixations seen in the colored photomicrographs.

The second part of the book is devoted entirely to the normal cells of blood and bone marrow, as well as lymphoid tissue cells. The third part discusses the erythrocytes, the pathology of the erythrocytes, and the various diseases associated with abnormal erythrocytes. There is discussion of the pathology of the leukocytes in leukemias, lupus, and also the various hereditary anomalies. The lymphosarcomas and granulomatous cells are discussed in this same section. The thrombocytes have a section entirely of their own, as does the reticulo-histiocytic system and parasites of the blood. The last chapter discusses tumor metastasis in the hemopoietic organs.

Photomicrographs of the cells are nicely done. My one criticism is that the plates and the discussion of the plates are in one section of the book and do not run concurrently with the description of the condition with which they are associated. It takes a little time and effort to page back and forth and keep the continuity of the discussion. In his preface, Dr. Dameshek states that the paintings are better than the photomicrographs that the average person is able to make.

By and large the book is well done, is a good reference book, and is certainly valuable for those interested in hematology.

E. N. NELSON, M.D.
Minneapolis

Current Diagnosis and Treatment

by HENRY BRAINERD, SHELDON MARGEN, *and* MILTON J. CHATTON, *870 pp., ill., Lange Medical Publications, Los Altos, Calif., 1964. $9.50*

"It is better to be brief than tedious," mutters one of Shakespeare's villains. Here is a book to reaffirm the wisdom of this homily—a concise review of medicine which modestly disclaims the status of a textbook but which often merits the title.

For example, comparison with larger volumes will not disclose a better section on treatment of hypochromic anemia than is found in the chapter on blood diseases. Again, the review of psychiatric diseases avoids the clichés without losing sight of basic terms. Here, inci-

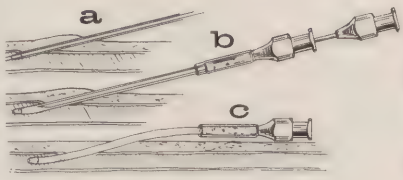
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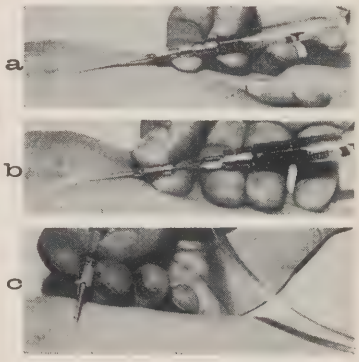
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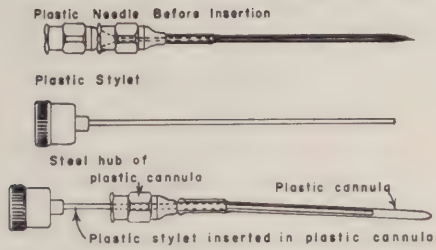




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Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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(Continued from page 16A)

dentally, the author warns that insight does not necessarily make a patient well.

Sometimes a section can be brief without being concise. A discussion of hearing difficulties could be improved by reediting the paragraphs on cerumen and by amplifying the material on hearing aids. A helpful appendix contains a glossary of genetic terms and a description and interpretation of chemical analytic procedures. The excellent section on pharmacology could be amplified with a description of specific drug idiosyncracies.

This book is inexpensive, bound as a large paperback with lithographed text and a few illustrations. Pages are attractive and easy to read. The bibliography is current and ample. I recommend this book for every practicing physician.

FRANK ANKER, M.D.
Oakland, Calif.

Advances in the Treatment of Menstrual Dysfunction

edited by ALVIN F. GOLDFARB, *188 pp., ill., Lea & Febiger, Philadelphia, 1964. $4*

This book is attractive, and it reads sensibly. It is an excellent book for all physicians who want to know what advances are being made in the way of helping women who have troubles with ovulation, menstruation, metabolism, fertility, endometriosis, or a failure to develop properly. The book is well illustrated. The chapters are brief and the text is to the point.

The several chapters have been written by experts. Many readers will be interested in the article on dysmenorrhea. Of late, much work has been done on this problem and especially on the use of hormones such as the estrogens, progesterones, and corticosteroids. Unfortunately the impression one gains is that even the gynecologists do not always know how to use these drugs to the greatest advantage. I know that of late I have tried to read and understand some of this literature but have found it hard going.

WALTER C. ALVAREZ, M.D.
Chicago

A Marriage Manual for Catholics

by WILLIAM A. LYNCH, *359 pp., Trident Press, New York City, 1964. $4.95*

If Dr. Lynch had written this book with the intention of revealing his own breadth of sociologic understanding it would be an entirely successful issue. When presented as a practical guide for couples who are building a marriage, however, it has overwhelming shortcomings, which make it impossible for me to recommend the book. Dr. Lynch sets an unreasonably high standard of sexual performance for his readers, strongly implying in many sections that a 100% orgasm response among wives is attainable by all couples. He gives virtually no specific advise on sexual technique in initiating or developing the physical side of the relationship. Worst of all, the book seems to me "preachy" in tone and neither empathetic nor noncritical in its viewpoint.

JOHN E. EICHENLAUB, M.D.
Minneapolis

News Briefs . . .

North Dakota

DR. ROBERT D. STORY, a staff member of the Fargo Clinic, has been appointed governor of the American College of Cardiology for North Dakota. A native of Valley City, Dr. Story received his medical degree from the University of Chicago in 1947. He is a member of the American College of Physicians, American Society of Internal Medicine, and the American College of Cardiology.

* * * *

DR. WILLIAM T. FERGUSON has joined the Dakota Clinic in Fargo in the department of orthopedic surgery. A native of Detroit, Dr. Ferguson graduated in 1956 from the University of Michigan Medical School and interned at Harper Hospital in Detroit.

* * * *

DR. MICHAEL J. BARNES of Ellendale has announced plans to leave for Hankinson, where he has purchased a practice. A native of England, Dr. Barnes received his medical education in London. He moved to Ellendale after having a general practice in Estevan, Sask.

* * * *

OFFICERS of the First District Medical Association in eastern North Dakota have been announced for 1965. They are Drs. Joseph F. Schneider, president; Blaine F. Amidon, vice-president; and Marshall Landa, secretary-treasurer.

* * * *

DRS. SAMUEL E. SHEA, JR., and B. JAYAPATHY, Minot otolaryngologists, will open a clinic practice in Williston. Both are members of the McCannel Clinic in Minot and the new offices will be known as the McCannel Ear, Nose and Throat Clinic, Williston Branch. The two physicians said they also will practice facial plastic surgery.

Minnesota

THE SIXTY-FOURTH ANNUAL CONVENTION of the American Proctologic Society will be held June 14-16 at the Hotel Leamington in Minneapolis. Scientific sessions of the meeting are open to all members of the medical profession. Requests for information should be directed to the secretary: James A. Ferguson, M.D., 320 West Lafayette Avenue, Detroit, Mich. 48226.

* * * *

DR. C. WALTON LILLEHEI, professor of surgery at the University of Minnesota, has been named president-elect of the American College of Cardiology. He will take office at next year's annual meeting in Chicago.

* * * *

DR. THOMAS C. LEACH has joined the staff of the Babbitt Medical Clinic in Virginia. A graduate of the University of Minnesota Medical School, Dr. Leach interned at Ancker Hospital in St. Paul and was in private practice in Minneapolis.

* * * *

DR. JOHN C. CAMPBELL, a native of Scotland, has joined the staff of the Albert Lea Medical and Surgical Center

(Continued on page 22A)



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NEWS BRIEFS

(Continued from page 21A)

as surgeon and urologist. Dr. Campbell, who received his M.D. from the University of St. Andrews in 1944, is a member of the Royal College of Surgeons, the Royal Society of Medicine in London, the American College of Surgeons, and the Canadian Urological Association.

* * * *

DR. ROBERT R. COOPER has been elected chief of staff of Fairview Hospital in Minneapolis. An ophthalmologist, Dr. Cooper is a 1946 graduate of the University of Minnesota Medical School. Other new officers are Drs. Meyer S. Belzer, chief-elect; John A. Hartwig, secretary; and Henry E. Brandt, treasurer.

* * * *

DR. CLARENCE A. SMITH of Edina has begun his duties as the new Commissioner of Health for Minneapolis. Dr. Smith, whose career in public health covers a period of twenty-eight years, is a 1935 graduate of the University of Colorado School of Medicine and a specialist in dermatology.

* * * *

DR. DONALD E. STEWART, Crookston surgeon, has been named a member of the American Cancer Society's national crusade committee. He will serve a two-year term as one of 18 committee members from across the United States. Dr. Stewart already is the professional delegate from Minnesota to the society's national board of directors. A native of Duluth, Dr. Stewart was graduated in 1938 from the University of Minnesota Medical School.

* * * *

DR. HOMER H. HEDEMARK of Ortonville has been elected a fellow of the International College of Surgeons. Dr. Hedemark was graduated in 1933 from St. Louis University School of Medicine.

* * * *

DR. CHARLES R. PELZL, Pine River, was selected as one of the 100 outstanding Minnesotans to be recognized at the "Republicans Care" awards luncheon in February. Dr. Pelzl was cited for his services to the people in Pine River and surrounding communities.

* * * *

DR. DONALD O. OSBORN, a member of the George A. Hormel and Co. medical staff in Austin, is leaving to join a private industrial clinic in St. Louis. A 1946 graduate of the University of Nebraska College of Medicine, Dr. Osborn is a fellow of the Industrial Medical Association and vice-president of the Minnesota Academy of Occupational Medicine.

* * * *

DR. HOMER RUSS of Lindstrom has announced plans to establish a practice in Warroad. Dr. Russ received his medical training at the University of Minnesota where he was graduated in 1959. He interned at Bethesda Lutheran Hospital in St. Paul.

South Dakota

DR. LAWRENCE E. SAVAGE has joined the Yankton Clinic as a general surgeon. Dr. Savage was graduated in 1956 from the University of Chicago School of Medicine and interned at Sacred Heart Hospital in Yankton.

* * * *

DR. L. EDGAR BOSTIAN of Sioux Falls has been appointed clinical director at the Northeastern South Dakota Mental

(Continued on page 24A)



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WANTED DOCTOR to locate in city of 1,000 in Red River Valley of North Dakota. Fine modern medical building. New 60 bed Nursing Home to be completed September 1st. Financial help and housing available. Reply to Harley Nash, Sec'y., Hatton Medical Center, Hatton, N.D.

WANTED—Young (30-35) general surgeon, Board eligible or qualified, to associate with group of general practitioners, North Dakota. Offering generous salary and early full partnership. Reply Box 29, c/o Journal Lancet.

WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED—Locum tenens—Pediatrician for one year, Multi-specialty group, northern Minnesota. Salary open. Northwestern Clinic, Crookston, Minnesota.

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WANTED—A General Practitioner to join a clinic group in Northeast Iowa town of 75,000. Excellent opportunity, good starting salary with partnership arrangements available. Excellent school system and a real nice city in which to live. Write: G. W. Glenn, Business Manager, Waterloo Surgical and Medical Group, 1125 West Fourth Street, Waterloo, Iowa 50702.

WANTED—General Practitioner in Jamestown, North Dakota. 14 man Multi-specialty group with general practice section. Starting salary $12,000, plus fringe benefits of insurances, vacations, pension plan, time off for post graduate training. Reply to Box 951, Jamestown, North Dakota.

NEWS BRIEFS

(Continued from page 22A)

Health Center. Dr. Bostian graduated in 1949 from Marquette University School of Medicine and interned at Milwaukee County General Hospital. He is a member of the American Psychiatric Association.

* * * *

DR. CHARLES J. MC DONALD, Sioux Falls general practitioner, has been reelected president of the Sioux Valley Medical Association. Dr. McDonald, a member of the American Academy of General Practice, graduated in 1933 from Creighton University School of Medicine.

Deaths . . .

DR. ALBERT E. OLSON, 69, prominent Duluth surgeon died Feb. 17. A former University of Minnesota regent, Dr. Olson graduated in 1920 from the University of Illinois College of Medicine as valedictorian of his class. He was a life member of the American College of Surgeons and had studied at various surgical clinics in Europe.

* * * *

DR. CARL ALBION WITHAM, 83, Edina, died March 10. Dr. Witham was a 1906 graduate of the University of Minnesota Medical School and a member of the American College of Surgeons. He was an honorary staff member at Methodist Hospital and an active staff member at Lutheran Deaconess Home and Hospital.

* * * *

DR. DAVID M. SIPERSTEIN, 67, Minneapolis, died March 11. Dr. Siperstein was an associate professor of pediatrics at the University of Minnesota and also was chief of staff of pediatrics at Mt. Sinai Hospital. He was a 1921 graduate of the University of Minnesota Medical School and a member of the American Academy of Pediatrics, Minnesota Pediatrics Society, Alpha Omega Alpha, and Sigma Psi.

* * * *

DR. LOUIS A. NELSON, 89, retired St. Paul physician, died March 10. A member of the American Academy of Ophthalmology, Dr. Nelson received his medical degree from the University of Minnesota in 1896. He was born in Lanesboro and lived in St. Paul for eighty-five years.

* * * *

DR. J. LAWRENCE NOBLE, 56, St. Paul, died March 8. Dr. Noble graduated in 1934 from the University of Minnesota Medical School. He was a member of the American Academy of General Practice and served on the staff of Bethesda Lutheran Hospital.

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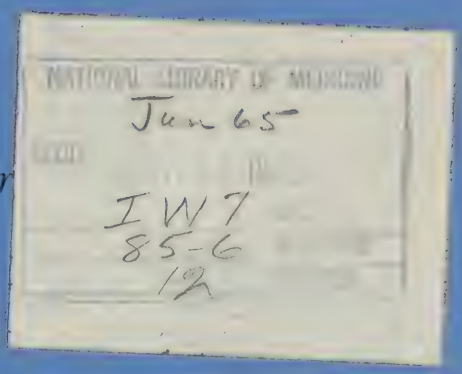
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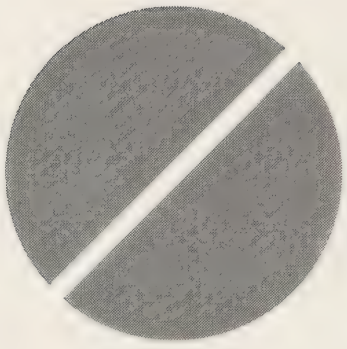


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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, *22*:527, 1964.

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*Neyroud, M.: Praxis 44:648-650 (July 14) 1955.

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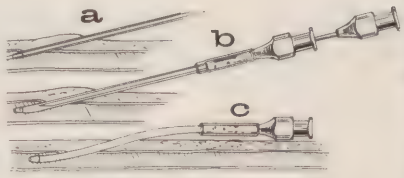
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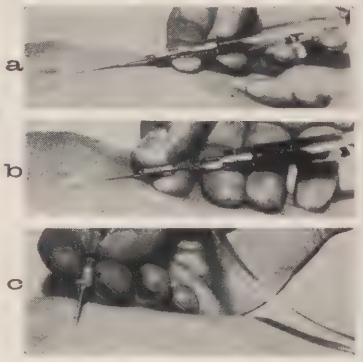
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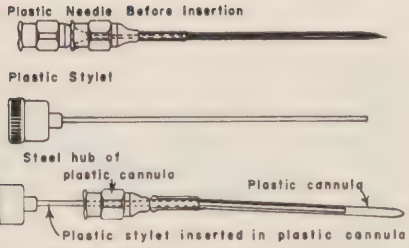




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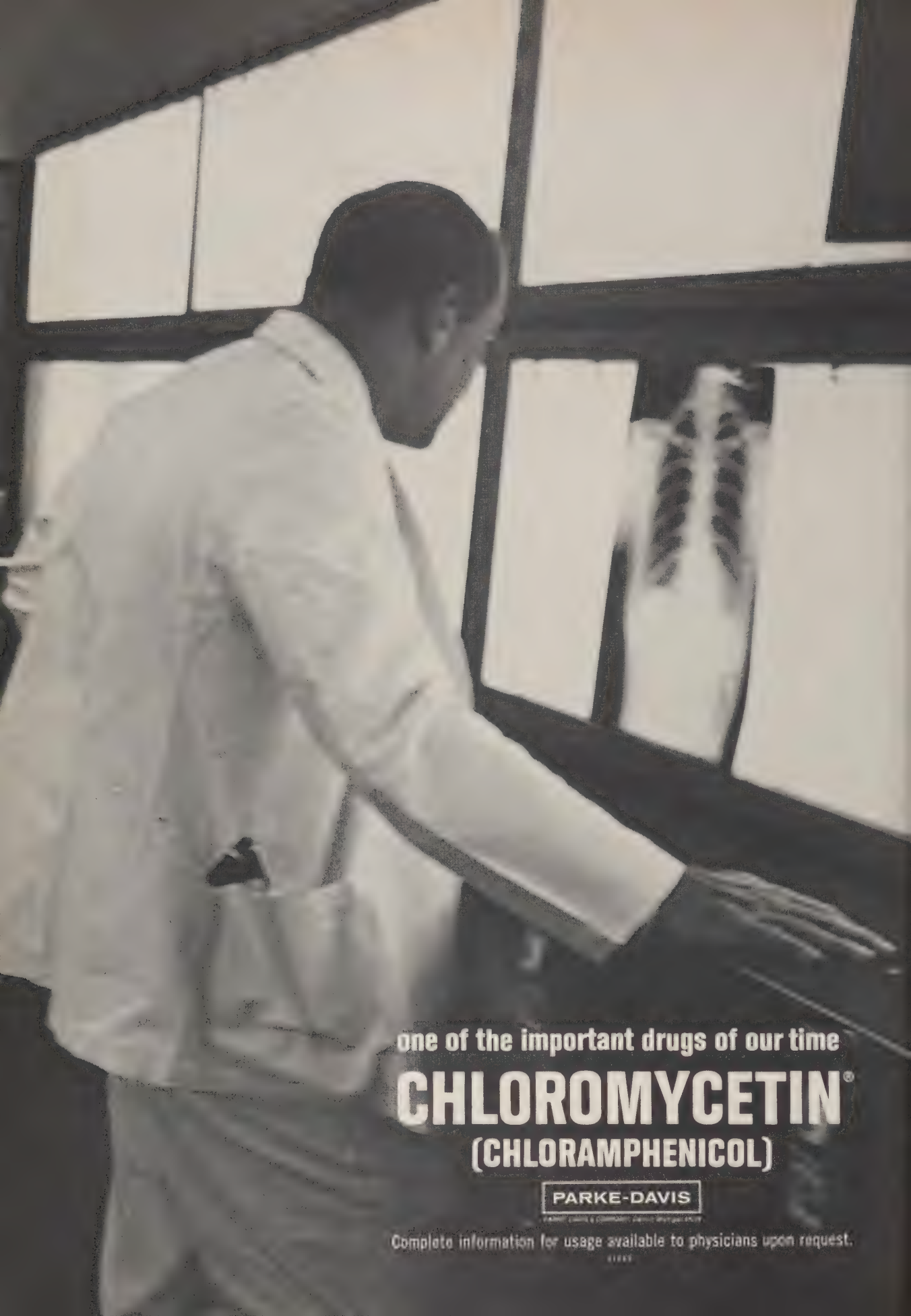
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Also in the July issue:

"Mesodermal Mixed Tumors," by R. F. Nuessle, M.D., Bismarck. Dr. Nuessle is with the department of surgery of the Quain and Ramstad Clinic. His article is a case report of a rare condition. Prognosis is poor but occasionally patients, such as the one he describes, survive longer than the average one year most often reported.

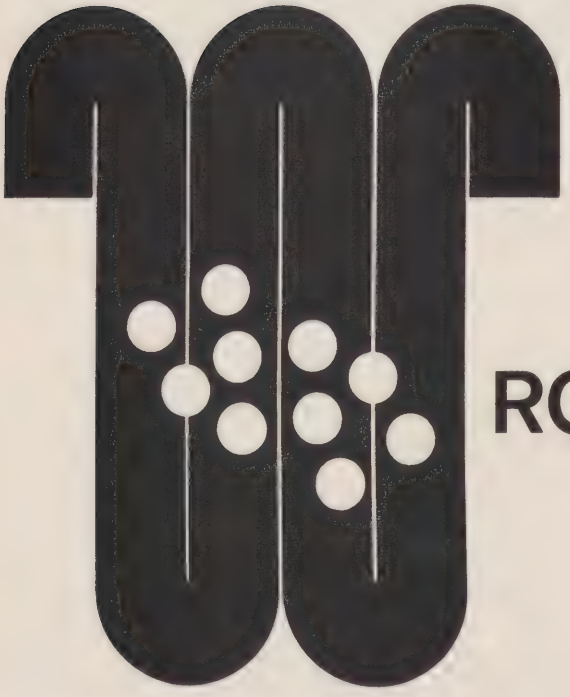
"Present Trends in Coronary Disease," by Paul D. Redleaf, M.D., St. Paul. Dr. Redleaf, clinical instructor, department of medicine, University of Minnesota, stresses application of present knowledge from fundamental, clinical, and epidemiologic investigations that some overt disease may be prevented and that established disease may be recognized earlier and treated more effectively.

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Milwaukee Children's Hospital

Special Issue on Pediatrics Marquette University

FORWARD

It is with pleasure that the department of pediatrics of Marquette University School of Medicine and the Milwaukee Children's Hospital join with the editors to present an issue of THE JOURNAL-LANCET.

The articles which follow represent a segment of the current studies of the staff, and together they tell something about the involved institutions and their activities.

As a young and growing department of pediatrics, we look forward to an ever-increasing role, along with other pediatric departments and physicians of the North Central United States, in the provision of care for children; in the teaching of students, interns, and residents; and in the conduct of research in the health problems of children.

J. C. PETERSON, M.D.

J. C. PETERSON *is chairman of the Department of Pediatrics, Marquette University School of Medicine, and Pediatrician-in-Chief at the Milwaukee Children's Hospital, Milwaukee.*

Hemorrhage in the Newborn

ARMAND J. QUICK, M.D.
Milwaukee

THE MYSTERIOUS BLEEDING occasionally observed in the newborn was most likely the first hemorrhagic state that came to the attention of man. One may speculate that the Mosaic law fixing the time of circumcision on the eighth day was not accidental but came about from the observation that when the rite was performed earlier bleeding often occurred.

The first clinical description of a case of bleeding in the newborn was reported by Mauriceau[1] as early as 1694. Two hundred years later Townsend[2] recognized the condition as a clinical entity, usually self-limiting and distinct from hemophilia. In 1937 Brinkhous and associates[3] reported that the prothrombin in normal newborn babies was much lower than in adults, and in one particular infant who was bleeding it was exceptionally low. Two years later Waddell and coworkers[4] were first to associate hypoprothrombinemia as measured by the one-stage test with vitamin K deficiency. In that same year 4 groups of investigators[5–10] independently observed that prothrombin of the blood was normal at birth, decreased during the first few days of life, and usually returned to normal within a week. As a result of these and other studies, effective treatment with vitamin K was established, methods of diagnosis developed, and means of prophylaxis introduced. These practical contributions have stood the test of time, but the advances made during the past twenty-five years in the study of blood coagulation now make it possible to attain a more complete understanding not only of the hemorrhagic disease of the newborn but also of other types of bleeding disorders in the neonatal period.

Bleeding in the infant, as in the adult, can be classified for convenience as spontaneous and traumatic. This is by no means an absolute distinction because there is much overlapping. The newborn infant, being well protected from trauma, may show no signs of a bleeding tendency, as in the case of hemophilia, for weeks or even longer. Gross trauma such as circumcision, however, promptly discloses the bleeding tendency. Two conditions in the newborn in which spontaneous bleeding is characteristic are severe hypoprothrombinemia and thrombocytopenia. These two states account for nearly all the bleeding encountered in the early neonatal period.

HEMORRHAGIC DISEASE OF THE NEWBORN

The term employed in the above title is reserved for the specific clinical entity caused by vitamin K deficiency which results in a decrease of prothrombin activity as measured by the one-stage prothrombin time test. Obviously, the crux in understanding the disease lies in the meaning of prothrombin activity. It is therefore desirable to review briefly the principle underlying the one-stage prothrombin time which is the key diagnostic test. It is established that when a properly prepared thromboplastin reagent is employed, the one-stage test yields a remarkably constant value of twelve seconds for normal human plasma. It has been shown that a decrease of prothrombin and factor V, VII, or X will cause the prothrombin time to increase. Since newborn plasma has the same prothrombin time of twelve seconds as adult plasma, none of the factors of the prothrombin complex appears to be significantly altered. How then can one explain the finding that the prothrombin measured with the Iowa two-stage method is only about 25% of the adult level?

To find an answer to the enigma, the results of a few simple experiments such as presented in the table are helpful. When citrated adult plasma is stored in glass at 4° C. for twenty-four hours, the prothrombin time decreases to nine seconds, indicating a marked increase of activity, while newborn plasma fails to show any change on storage. In the next series of experiments it will be noted that when either adult or newborn plasma is diluted with an equal volume of saline, the resulting mixture has a prothrombin time of fifteen seconds. When the diluent is normal plas-

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ma adsorbed with $Ca_3(PO_4)_2$, the mixture with adult plasma has a prothrombin time of twelve seconds, while that of the newborn is fifteen seconds. In analyzing these findings, factor V and fibrinogen may be dismissed since both are normal in newborn plasma and neither one is adsorbed by $Ca_3(PO_4)_2$. Obviously, adult plasma contains a factor which is not present in newborn plasma. This factor appears to be in an inactive form in fresh plasma which becomes active on storage in glass. Adsorbed plasma is completely devoid of prothrombin and factors VII and X, but it must contain some principle which reacts with the inactive factor in adult plasma to restore the prothrombin time of the mixture to twelve seconds. This strongly suggests that it is a reactant—not an accelerator. Evidence has been presented indicating that its concentration is genetically determined[11] and the name "prothrombin time fixing agent" (PTFA) has been proposed.[12] The inactive factor which PTFA converts to the free form could theoretically be a precursor of prothrombin, factor VII or X. Since prothrombin as measured by the two-stage method is low in newborn plasma, it is this factor which appears most likely to be in a precursor state. Thus, newborn blood which is low in prothrombin shows no increased activity on storage. It has therefore been postulated that all of the prothrombin in adult plasma is in the precursor state except the fraction made active by PTFA and that only the latter affects the prothrombin time. In adult blood, 75% of the total prothrombin is inactive, whereas newborn blood has the same concentration of free prothrombin but lacks prothrombinogen. This explains why the one-stage prothrombin time is twelve seconds, the same as in adult plasma, and why it shows no shortening of the prothrombin time when stored in glass. In adult plasma, storage activates all the prothrombin, hence the marked decrease of the prothrombin time. The latter value is actually a measure of the total prothrombin. The prothrombin time of fresh plasma measures only the fraction of the prothrombin which is in the active state, whereas the two-stage method measures total prothrombin but does not distinguish between the free and the inactive forms.

According to this concept the newborn has the same concentration of free prothrombin as adult plasma but is devoid of the prothrombin precursor. Thus, the baby has a normal prothrombin but a marked hypoprothrombinogenemia. This, as such, does not affect the infant's hemostasis but it does make it more prone to develop a bleeding state. Prothrombinogen may be regarded as a storage reserve which the young infant does not have. Apparently the formation of prothrombinogen requires time because the total prothrombin attains the adult level only after several months.

PROTHROMBIN IN ADULT AND NEWBORN PLASMA

EFFECT OF STORAGE

*Plasma**	*Prothrombin time*	
	Fresh (seconds)	*After storage in glass† (seconds)*
Adult	12	9
Newborn	12	12

EFFECT OF DILUTION

Plasma		*Prothrombin*	
		One-stage method (seconds)	*Two-stage method %*
Normal adult		12	100
Newborn		12	25
Normal adsorbed with $Ca_3(PO_4)_2$		infinity	0
Normal adult Saline	1 vol. 1 vol.	15	50
Newborn Saline	1 vol. 1 vol.	15	12.5
Normal adult Normal adsorbed	1 vol. 1 vol.	12	50
Newborn Normal adsorbed with $Ca_3(PO_4)_2$	1 vol. 1 vol.	15	12.5

*Citrated plasma is employed because on short-term storage, little of factor V is lost.

†Storage is for twenty-four hours at 4° C.

The proneness with which the newborn develops a deficiency of vitamin K is due first to the lack of a storage reserve of the vitamin in the fetus, secondly to the low intake during the first few days, and thirdly to the high metabolic demands for this vitamin which greatly exceed the adult requirements. Quick, Collentine, and Hussey[13] found that the growing pup required a maintenance dose which is 25 to 50 times higher than that of the adult dog. The newborn almost invariably has some degree of hypoprothrombinemia during the first several days of life and occasionally has a slightly defective hemostasis which manifests itself only when trauma occurs. Because the newborn lacks any reserve of either prothrombin or vitamin K, a mild vitamin K deficiency easily becomes severe with the result that a full-blown hemorrhagic disease of the newborn can readily develop.

One may assume that in vitamin K deficiency of the newborn, the sequence is essentially the same as in the adult except that it is more drastic because the reserve prothrombinogen is lacking. The first agent that becomes reduced is factor VII, and as it decreases prothrombin drops.

There is also a reduction of factors IX and X but these are difficult to measure quantitatively.

The basic one-stage method is not specific for any one of the factors grouped under the prothrombin complex but with a slight modification, namely, adding a small quantity of aged serum to the plasma, it becomes a quantitative measure of prothrombin because serum supplies factors VII and X but no prothrombin. Thus, by means of the basic one-stage test and the simple modification, prothrombin can be differentiated from factors VII and X.

Because the newborn under normal environment and with good nutrition in the mother may nevertheless have a slight but demonstrable and transient hypoprothrombinemia unless either the mother or baby received extra vitamin K, it is not surprising that Vietti and associates[14] found the incidence of postcircumcision bleeding considerably higher in babies who did not receive extra vitamin K. In all the babies that bled, the prothrombin time was significantly elevated. These and the findings of others clearly demonstrate that, in moderately depressed prothrombin activity, a bleeding tendency is present but not manifested unless injury or trauma is superimposed. As the hypoprothrombinemic state progresses the susceptibility to bleeding after injury increases and eventually reaches a point at which hemorrhage becomes spontaneous. Attempts to attribute the bleeding to any one factor of the prothrombin complex have been fruitless. Spontaneous bleeding is known to occur in severe hereditary pure hypoprothrombinemia[15] and also in factor VII and X[16] deficiencies. In severe hypoprothrombinemia of the newborn, all 3 factors are reduced. Even if each of these factors could be measured specifically with unequivocal precision, it would still be almost impossible to determine whether any one of these 3 is more responsible for the breakdown in hemostasis than the other 2 or whether the effect is a composite one involving all 3. Because of this complexity, the basic one-stage test has remained the best guide to diagnosis, to gauge the severity and to evaluate the therapeutic response to vitamin K.

NEONATAL THROMBOCYTOPENIA

It is likely that in conditions of good nutrition platelet deficiency is the most common cause of bleeding in the early neonatal period. Anthony and Krivit[17] state that "Thrombocytopenia in the newborn infant is probably more common than the numerous case reports in the literature would indicate." Thrombocytopenia of the newborn may be hereditary or acquired. The first is rare so that most of the reported cases are probably of the immune type in which a platelet antibody present in the mother's blood is transferred through the placenta. The recent observation of Rodriguez and his co-workers,[18] who associate neonatal thrombocytopenia with antepartum administration of thiazide drugs, introduces a new facet of the problem, namely, the depression of thrombopoiesis in the fetus by drugs given to the mother.

Irrespective of the cause, the bleeding in thrombocytopenia is of the spontaneous type. Characteristically, petechiae are almost invariably present and bleeding from mucous membranes occurs. In the very severe form, the fetus may show petechiae, intracranial hemorrhages, and other types of bleeding which are obviously not traumatic but spontaneous.[19] Because spontaneous bleeding is the typical form in thrombocytopenia, intracranial and intraocular hemorrhages occur with much greater frequency than in any other bleeding disorder.

The diagnosis of neonatal thrombocytopenia is easily made. The presence of petechiae suggests the type of bleeding and this is verified by a platelet count. It is important to find the cause. Therefore, in taking the medical history, questions should be directed toward the possibility of a bleeding tendency in the family, the occurrence of idiopathic thrombocytopenia in the mother, and the nature of the drugs given antepartum, especially of the thiazide group.

HEREDITARY HEMORRHAGIC DISORDER

Surprisingly, neonatal bleeding is rarely encountered in hemorrhagic disorders that are of hereditary origin. Dr. Hussey and I reported one case of hereditary thrombocytopenia in which severe bleeding was present at birth.[20] Bachmann studied an infant in whom hemorrhagic disease of the newborn complicated a severe hereditary deficiency of factor X,[21] and Rabiner and his associates[22] found a similar situation except that the hemorrhagic disease of the newborn was superimposed on a hereditary factor VII depression. I am not aware of any recorded spontaneous bleeding during the first few days of life in hemophilia, hereditary hypoprothrombinemia, von Willebrand's disease, or any other authentic severe hereditary bleeding disorder. Even umbilical bleeding is rarely seen. These diseases, therefore, present little or no problem in the neonatal period, in fact, not until the baby becomes subject to slight trauma which is usually first encountered when the crawling stage begins or the first teeth erupt.

When bleeding occurs in the newborn, vitamin K should be given immediately and a sample of

blood obtained for diagnostic study. If blood cannot be obtained by venipuncture, a microprothrombin time should be made on capillary blood. Should the diagnosis be hypoprothrombinemia, no time has been lost, and if the tests indicate a different diagnosis, no harm has been done. As a matter of fact, vitamin K may be regarded as beneficial in all types of neonatal bleeding because it effectively prevents or corrects the transient physiological hypoprothrombinemia which occurs even in normal infants. Thus, vitamin K guards against superimposing a hypoprothrombinemic state on the other basic hemostatic defect.

SUMMARY

The classical hemorrhagic disease of the newborn is caused by vitamin K deficiency. It is recognized by a markedly prolonged one-stage prothrombin time. The concentrations of factors VII, IX, X, and prothrombin are reduced. The disorder responds promptly to vitamin K and can be prevented by supplying the infant with this vitamin. Thrombocytopenia is the second important cause of bleeding in the neonatal period. It is usually caused by a platelet antibody transferred from the mother's blood through the placenta. Hereditary bleeding diseases such as hemophilia rarely cause bleeding during the first few days of life unless trauma such as circumcision is induced.

This work was supported by a grant from the National Heart Institute, National Institutes of Health, U.S. Public Health Service.

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THE MOST EFFECTIVE TREATMENT for chronic ulcerative colitis is early total proctocolectomy and ileostomy. The operation is performed for lack of response to medical management in about one-fifth of patients. These patients often have secondary indications such as chronic hemorrhage and colonic or rectal stricture. Operation is indicated for complications such as fistula, polyposis, obstruction, perforation, hemorrhage, and infantilism. Perineal, enterocolic, or colocutaneous fistulas comprise nearly half the complications encountered. Operation is indicated for suspected malignant condition. Recurrence rate is high with subtotal colectomy and is also a threat in partial colectomy, ileostomy, colostomy, or ileocolostomy. More than 90% of patients survive early total proctocolectomy and ileostomy and more than 90% of these make good or excellent recoveries.

JOHN M. WAUGH, M.D. (deceased), DONALD A. PECK, M.D., OLIVER H. BEAHRS, M.D., and WILLIAM G. SAUER, M.D., Mayo Clinic and Foundation, Rochester, Minn. Arch. Surg. 88:556-569, 1964.

Postrubella Thrombocytopenic Purpura

Report of Nine New Cases and Review of Published Cases

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While due attention has been paid to postrubella embryopathy, encephalitis, and arthritis, a fourth complication of rubella, thrombocytopenic purpura, is rarely mentioned. Indeed, it is notably absent from discussions of both rubella and thrombocytopenic purpura in the 1964 edition of Nelson's Textbook of Pediatrics. A very recent experience with 9 patients with postrubella thrombocytopenic purpura during the height of an epidemic has directed our interests to this problem.

Since the first well-documented case report by Pitten[1] in 1929, a scant 30 new cases of postrubella thrombocytopenic purpura have appeared despite the ubiquitous nature of rubella. Ferguson,[2] in 1960, reviewed 19 patients, including 2 of his own, drawing from the experiences of 10 authors. From this excellent review came the first substantial knowledge of its clinical features. Tadzer,[3] in 1958, added 6 patients. This report was notable for the careful investigation of plasma coagulation factors, capillary fragility, and the search for antiplatelet antibodies. Cohen[4] reported a single patient in 1960. The final contribution of 5 patients was made by Wallace in 1963.[5]

The City of Milwaukee Health Department, in 1964, reported the highest incidence of reported rubella cases in the past ten years (Table 1). During the height of the epidemic, 12 infants and children were admitted to Milwaukee Children's Hospital for evaluation of thrombocytopenic purpura, following suspected rubella infection. None of these children had had previously known bleeding or bruising tendencies. Family histories were also unrevealing for hemorrhagic disease.

A definite history of preceding rubella infection could be obtained in 10 patients. One patient had clinical and laboratory evidence of concurrent beta streptococcal infection and was eliminated from this report. The remaining 9 included in this report are shown in table 1 to have increased our ten-year experience with this problem by 300%. Table 2 demonstrates that these cases did indeed occur at the height of the epidemic.

A summary of some of the clinical features exhibited by this group of patients is shown in table 3.

CASE REPORTS

Case 1. A 4-year-old boy developed rubella on June 24, 1964. His initial illness was mild, unmarked by fever, with the rash fading on the third day. On the sixth day, June 29, 1964, his mother noted a petechial rash on the lower extremities, with bruises over both knees and left palm. Because of increasing purpura he was seen by his pediatrician and admitted to Children's Hospital on the eighth day, July 1, 1964. Admission examination revealed an active 4-year-old boy who did not appear ill despite a generalized petechial rash, maximal on his lower extremities, with involvement of oral mucous membranes. There was no evidence of hepatosplenomegaly or

TABLE 1

Year	*Reported rubella**	*Postrubella thrombocytopenic purpura†*
1955	732	
1956	5053	1
1957	2778	
1958	16441	1
1959	1028	
1960	1057	
1961	1076	
1962	687	1
1963	1325	
1964	30858	9

*City of Milwaukee Health Department
†Admitted to the Milwaukee Children's Hospital

HOWARD LOKIETZ *and* FRANK A. REYNOLDS *are with the Milwaukee Children's Hospital.*

TABLE 2

Month	Cases rubella*	Postrubella thrombocytopenic purpura†
January	247	
February	951	
March	4347	
April	9491	1
May	9781	5
June	4909	2
July	755	1
August	154	
September	95	
October	71	
November	57	

*Reported to Milwaukee Health Department
†Admitted to Children's Hospital

lymphadenopathy. Initial platelet count was 6,000 with a positive Rumpel-Leede test and a Duke bleeding time of twelve minutes. Three urine specimens showed no protein. There were only occasional red cells on 2 specimens. By the tenth day his platelet count had risen to 38,000. No new purpuric lesions were noted after the eleventh day when he was discharged. Follow-up office visit on the fifteenth day demonstrated that all lesions had disappeared with the exception of fading ecchymoses over his knees. Platelet count at this time was 183,000. He has had no recurrence of purpura since that time.

Case 2. A 6-year-old girl developed rubella May 3, 1964, with the rash fading by the third day. Apparently recovered, she resumed school activities on the fourth day, but on return home that afternoon was noted to have large bruises on her arms, legs, and trunk. During the next twenty-four hours the purpura became more intense, leading to hospitalization on the fifth day, May 7, 1964. She was in no distress despite an initial temperature of 101.4° rectally, and extensive ecchymoses over extremities and trunk with petechial showers over the lower legs and oral mucosa. Prominent posterior cervical nodes were found. The spleen was not palpable. The Rumpel-Leede test was strongly positive. Initial laboratory studies disclosed a platelet count of 8,000, a Duke bleeding time of nine and one-half minutes, and a Lee-White clotting time of twelve minutes, forty seconds. Within eight hours after admission gross hematuria with passage of clots became evident. This paralleled the appearance of new ecchymoses and resulted in a marked anemia within a period of five days.

Bone marrow examination on the ninth day, May 11, before institution of steroid therapy, disclosed an active marrow with a slight megakaryocytosis, but poor platelet production and thrombocytopenia.

During the period of active urinary tract bleeding, the patient had mild loss of appetite but no other complaints. Within twelve hours of institution of steroids all evidence of active bleeding disappeared. Full steroid dosage was maintained through the next four-day period, with gradual withdrawal of steroids over a seven-day period, ending on day 21. She was well at office visits with platelet counts of 336,000 and 200,000 on days 27 and 34. There has been no recurrence of purpura in the past five months.

Day	Hgb.	HCT	Retic	Platelet	Urine	Treatment
6	11.5	35	1.2	8,000	Grossly bloody	None
9	7.5	22	—	14,000	Grossly bloody	Prednisone
10	6.0	20	5.8	14,000	Clear urine	60 mg. per M^2 per day
13	7.5	22	—	32,000	No micro, RBC, or protein	
14					Discharged on prednisone	

Case 3. An 8-year-old girl developed rubella May 4, 1964, with the appearance of multiple bruises on her trunk on the fifth day, May 8. The following day she sustained a mild blow to her left cheek resulting in a large hematoma. Spontaneous purpuric lesions continued

TABLE 3

Case	Age	Sex	Purpura interval[1]	Days duration	Bleeding site: Nose	Mouth	Urinary	Treatment[2]	Outcome
1	4 years	M	5	6	0	0	0	0	Recovered day 15
2	6 years	F	3	7	0	0	Gross	Steroid (9-21)	Recovered day 27
3	8 years	F	2	9	0	0	0	0	68,000 day 204
4	7 years	M	13	7	0	sl.	Gross	Steroid (16-23) Blood	156,000 day 23[3]
5	7 years	F	4	9	sl.	sl.	0	Steroid (8-25)	Recovered day 25
6	13 months	F	6	9	0	0	0	Steroid (16-25)	Recovered day 167[4]
7	23 months	F	9	6	0	0	Micro	Steroid (11-25) Blood X2	Recovered day 187[4]
8	5 years	M	6	8	Gross	0	0	Steroid (9-27)	Recovered day 29
9	12 years	F	15	9	sl.	sl.	0	Steroid (22-92)	Recovered day 174

1. Onset of rubella to initial purpura
2. Days of therapy inclusive
3. Lost to follow-up
4. First normal platelet count

to appear until admission to Children's Hospital on the eighth day, May 11. On admission she was noted to have a generalized petechial rash with ecchymotic areas on her trunk and left cheek. Moderate posterior cervical adenopathy was present. The spleen was not palpated. Initial platelet count was 18,000 with a three-minute Duke bleeding time and a negative Rumpel-Leede test. Urinalysis failed to show even occasional red blood cells. Bone marrow on day 10 revealed active myeloid and erythroid series with normal to slightly reduced numbers of megakaryocytes which rarely demonstrated associated platelets and a slight increase of marrow fat.

As there was no evidence of epistaxis or gastrointestinal or urinary tract bleeding, steroid therapy was withheld. There were no new purpuric lesions after day 11, despite a low platelet count which remained below 20,000 until day 20. The patient was asymptomatic and residual purpura was fading at the time of discharge on day 23 when 84,000 platelets were recorded.

Since discharge there has been no recurrence of purpura despite a persistent thrombocytopenia ranging from 40,000 to 80,000. The latest count on day 204 demonstrated 68,000 per cubic millimeter. She cannot be considered as recovered at this time.

Case 4. A 7-year-old boy developed rubella May 14, 1964, characterized by mild constitutional symptoms, a rash maximal on his head, neck, and upper trunk, fading in three days, and a single day of headache on the fourth day. He had apparently recovered from his illness when, on May 27, the fourteenth day, he suddenly developed oral bleeding, gross hematuria, and generalized purpura within a twelve-hour period. On admission the following day he was found to have slight persistent oozing from gingival tissue at the base of 2 carious teeth and generalized purpura. His spleen was not palpable. Initial platelet count was 6,000 with a five-minute Duke bleeding time. Because of continued gingival bleeding and gross hematuria, his pediatrician elected to transfuse the patient with 120 cc. of platelet rich blood, and to initiate full prednisone therapy of 60 mg. per square meter per day on day 16. Gross hematuria and gingival oozing ceased within five days of therapy, day 20, despite platelet counts of 2,000 and 4,000 on days 19 and 20. His urine was microscopically clear of red cells by day 23. A rapid rise in platelet count to 156,000 was noted on the same day as steroids were being withdrawn. He was unfortunately lost to follow-up when his parents moved shortly thereafter without a forwarding address.

A sample of marrow obtained day 19, after 4 days of steroid therapy, demonstrated marked megakaryocytosis with many ground glass forms and only a few demonstrating platelet production.

Case 5. A 7-year-old girl developed rubella May 15, with the onset of easy bruising on the fifth day, May 19. During the succeeding forty-eight hours the purpura became generalized. On day 7 she developed spontaneous oozing from her nasal mucosa and gums. Outpatient laboratory studies that day disclosed 15,000 platelets. Duke bleeding time was markedly prolonged with pressure required to achieve hemostasis at twenty-eight minutes. That evening she became febrile and was admitted the following day when the laboratory studies became available. She had generalized purpuric lesions on her trunk and extremities. There was slight oozing from both nares and oral mucosa. The spleen was not palpated. Marrow examination on the day of admission, day 8, revealed normal numbers of megakaryocytes, with decreased platelet production and thrombocytopenia. Prednisone 60 mg. per square meter per day was initiated. She continued to lose blood through steady oozing from her nose and mouth until day 11. The hematocrit had declined from 35% to 28% at that time. The first rise in platelet count of 68,000 was noted on day 13. A mild thirty-minute epistaxis on day 14 concluded all evidence of bleeding or purpura. Full prednisone dosage was continued after discharge until day 25, and discontinued on day 32. Recorded platelet counts on days 32 and 47 were 373,000 and 436,000, respectively. There has been no recurrence of purpura or bleeding in the past six months.

Case 6. A 13-month-old girl developed rubella June 16, with apparent recovery in three days. Petechial rash appeared on her extremities June 23, day 7. New lesions continued to appear over the succeeding days until admission on day 12. She was lethargic, with multiple petechiae on her extremities, mantle area, and soft palate and with ecchymoses over her left elbow and right pretibial area. The spleen tip was barely palpable. Initial platelet count on day 13 was 20,000, with a two-minute Duke bleeding time. The Rumpel-Leede test was slightly positive. There was no evidence of external blood loss or anemia. Because new petechiae continued to form during the next three days, her pediatrician elected to begin prednisone 30 mg. per square meter per day on day 16. The platelet count had spontaneously risen to 40,000 on that day. No new lesions were noted after day 18, and the platelet count had further increased to 94,000 by day 20. Prednisone was continued at home until day 25. Return office appointments were not kept, however, and this infant was not again seen until Nov. 30, day 167, when 298,000 platelets were counted. The mother denied further purpura during this interval.

Case 7. A 23-month-old girl developed rubella May 4, with mild fever and rash subsiding within three days. She was well when her mother observed petechial lesions on the oral mucosa the evening of May 13, day 10. The following morning the infant had generalized petechiae and ecchymoses. At admission on day 11 she was not ill and had no fever, adenopathy, or splenomegaly. The platelet count was 58,000 per cubic millimeter and a Rumpel-Leede test was slightly positive. Duke bleeding time was three and one-half minutes. There were 20 to 30 red blood cells per high-powered field in the urine. Two subsequent urine specimens showed no red cells or protein. Bone marrow examination on day 12 showed decreased numbers of megakaryocytes which did not appear to be producing platelets. Increased marrow fat suggested mild marrow depression although the maturation of the myeloid and erythroid series appeared normal. Prednisone 60 mg. per square meter per day was initiated on admission. The hospital course was uneventful and she was without new purpuric lesions after day 15, although the platelet count was 4,000 on that day. On the eighteenth and twentieth days the platelets were 60,000 and 23,000 per cubic millimeter, respectively. She was discharged on day 20 with prednisone until day 25. A platelet count on day 26 showed 78,000 per cubic millimeter. No further counts were made until Nov. 27, day 187, when a platelet count was 311,000. There had been no purpura from discharge to that time.

Case 8. A 5-year-old boy developed rubella July 1, 1964, with the rash fading in three days and unaccompanied by fever. On July 7, day 7, he received benzathene penicillin, 600,000 units intramuscularly, because

of known beta-streptococcal infection of the mother, together with the boy's complaint of sore throat that day. The injection site bled for five minutes. That evening he had two mild episodes of spontaneous epistaxis, and purpuric lesions were noted on his extremities and trunk. At admission the following morning, day 8, he had purpuric lesions, but his epistaxis had ceased. A Rumpel-Leede test was strongly positive. The initial platelet count was 6,000. The Duke bleeding time was 16 minutes. During the first four hospital days, days 9 to 12, he had brisk epistaxis despite prednisone 60 mg. per square meter per day and local measures. One thousand cubic centimeters of whole blood were required during this period to maintain the hemoglobin at the admission level of 11.5 gm. %. All bleeding and purpura ceased on day 14, although platelet counts were 10,000, 3,000, and 24,000 on days 15, 17, and 21 respectively. By the twenty-ninth day, off steroids for forty-eight hours, his platelet count had risen to 232,000. His last count two weeks later, day 44, was also within normal range at 248,000. There has been no recurrence of purpura or bleeding since discharge.

Case 9. A 12-year-old girl developed rubella April 10. She developed spontaneous bruising and a petechial rash. Despite the appearance of purpura she felt well and was not brought for medical attention until awakening the evening of April 30, day 21, with spontaneous bleeding from the mouth and nose. When admitted to Children's Hospital the following morning, she appeared well except for extensive purpura maximal on her extremities, with lesions on her trunk and oral mucous membranes as well. There was no external bleeding at this time. Initial platelet count was 24,000 with a ten-minute Duke bleeding time. Prednisone, 60 mg. per square meter per day, was started on admission. No further bleeding was encountered after admission, day 22, and no new purpura was noted after day 24. Despite this improvement, the platelet count remained below 38,000, with one count of 6,000 being recorded on day 50. She also had, at this time, early cushingoid facies from the continued high prednisone administration. A bone marrow examination of day 46, after twenty-four days of steroid therapy, showed increased fat content with megakaryocytopenia, none showing platelet production. The myeloid and erythroid series were considered normal.

Prednisone was continued at 45 mg. per square meter per day after discharge until day 92. The platelet counts during this time varied from 22,000 to 80,000. Prednisone dosage was reduced to 10 mg. per square meter per day, and was maintained to day 174. There was a gradual rise to 133,000 at this time. The last platelet count was 210,000 performed on the two hundred eleventh day of her illness. The course after hospitalization was free of purpuric manifestations.

DISCUSSION

Nine cases of postrubella thrombocytopenia purpura occurring during a single epidemic in Milwaukee during 1964 are presented. These, with the 12 cases[3–5] that have been reported since Ferguson's study of 19 well-documented cases in 1960,[2] bring the total documented cases to 40.

A subclinical form of thrombocytopenia without purpura has been noted. In various published reports, 55 patients described as having uncomplicated rubella had platelet counts done in the immediate postrubella period. Twenty-six of these patients demonstrated mild to moderate thrombocytopenia.[3,6–8] Tadzer also found increased capillary fragility in 20 of 36 patients in this category.[3]

Clinical postrubella thrombocytopenic purpura occurs exclusively during epidemics of rubella, during the spring or summer months.[2,5] There is no clear-cut sex difference—24 females, 16 males—although a small series such as our own, 6 females, 3 males, may imply this. The age incidence parallels the expected rubella susceptible population with 24 of 40 cases appearing in the 5- to 10-year age group. The youngest patient, age 1 year, (patient 6 in the present series) is the only reported case under the age of 2 years. Four cases are reported among young servicemen, 18 to 28 years of age.[6,9] The patients appear essentially well despite the dramatic appearance of the purpura. Palpable spleens are not the rule.

The interval between onset of rubella rash and the appearance of purpura has been as long as fifteen days, as in patient 9, but generally is six days or less, as with 26 of 34 patients.[2,4,5] A case in which the rubella rash and the purpuric lesions appeared simultaneously has been reported.[7]

The duration of purpura and hemorrhagic manifestations has varied from a single day to fifty-four days.[5] In most instances, however, it has persisted less than three weeks. In our present series of patients, the range was between six to nine days (Table 3). Twenty-eight of forty patients have been described appropriately for analysis of the site and severity of external blood loss.[2,4,5,10] Blood loss occurred from either nasal, oral, or urinary tract mucosa in 20 of these 28 patients. Gross bleeding requiring transfusion occurred in 9 patients. Gross hematuria occurred in 5 patients and microscopically in two.

Massive cerebral hemorrhage occurred in one patient, accompanied by hematuria, resulting in the only fatality in these 40 patients.

Almost uniform recovery is the rule in this disease. Our series is representative of the eventual excellent prognosis (Table 3). Torp and Steen[7] reported an exceptional case with persistent thrombocytopenia at seven months. Patient 3 has been observed for nearly seven months and shows a similar mild thrombocytopenia without purpuric symptoms.

MECHANISM OF PURPURA

Increased capillary fragility has been consistently noted in all series. Fragility is greatest at the onset of purpuric manifestations and does not correlate well with the platelet count. Fragility

TABLE 4

BONE MARROW EXAMINATIONS

Case	*Megakaryocytes*	*Platelet production*	*Free platelets*
2	Slight increase	Decreased	Few
3	Slight decrease	Rare	Few
4	Increased	Decreased	Few
5	Normal	Decreased	Few
7	Decreased	None	Rare
9	Decreased	None	Rare

may be increased for a significant period of time after normal platelet levels are present.[3]

Plasma coagulation factors are not deficient. A careful analysis of 6 patients by Tadzer demonstrates that the increased serum prothrombin time, sometimes seen in these patients, can be corrected by the addition of sufficient platelets.[3]

The mechanism of thrombocytopenia is poorly understood. Circulating platelet antibodies have been demonstrated in only 1 of the 9 patients in which they were sought.[2,3] The so-called "platelet loading effect" associated with viremia or bacteremia is quite transient[10] and does not explain the prolonged deficiency of circulating platelets.

In the present series, bone marrow examination was performed in 6 patients (Table 4). A significant effect on the megakaryocytes was noted in all cases with consistent finding of the inhibited platelet production. Wallace reports a similar picture in both marrows examined in her series.[5]

SUMMARY

Nine patients with thrombocytopenic purpura are described. All occurred during an epidemic and were admitted to the hospital during a two-month period at the height of the epidemic. The duration of purpuric and hemorrhagic manifestations did not exceed nine days in any patient. Seven of eight patients followed demonstrated complete recovery within six months. One patient is asymptomatic, but has continued to show a modest thrombocytopenia six months later. The clinical features of these nine patients and thirty-one previously reported patients are summarized.

The available information on the mechanism of purpura in postrubella thrombocytopenic purpura is mentioned. The consistent finding of poor platelet production in 6 marrow examinations suggests a primary effect on the megakaryocytic maturation in this disease.

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APPARENTLY-SOLITARY TUMORS of the vertebral column are predominantly malignant and, more often than not, are metastatic. The most prevalent primary tumor is chordoma, but the incidence of myeloma and chondrosarcoma also is high. With the exception of osteogenic sarcoma and Ewing's tumor, most malignant tumors occur after age 30, whereas the majority of benign neoplasms develop earlier. Even benign neoplasms that tend to recur locally are often fatal because of their nearness to vital structures. Early diagnosis and treatment are thus vital for all vertebral column tumors. The commonest initial symptom is pain, and roentgenographic findings usually are nonspecific. Prognosis varies with type of tumor.

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Ritter's Disease

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GOTTFRIED RITTER described an exfoliative dermatitis of the newborn in 1878[1] and in 1880[2] reiterated that he thought the disease was associated with puerperal infection. Elliott,[3] in 1888 the first to describe the disease in the English literature, doubted its pyogenic origin. In 1898 Winternitz[4] isolated staphylococcus from 2 cases and suggested this organism as the etiologic agent. Recent standard pediatric texts[5–7] do not implicate Staphylococcus aureus as the sole, or even as the main, etiologic agent. Recent reports,[8–13] however, have shown that Staph. aureus, group 2-phage type patterns, is the organism involved.

An epidemic in a local hospital in 1963 gave us an opportunity to study 8 cases, to review our hospital material, and to add observations supporting the role of Staph. aureus in the causation of this disease.

STUDY OF HOSPITAL EPIDEMIC

The infants born in the hospital in which an epidemic of Ritter's disease occurred were cared for in 1 of 4 nursery areas: a small unit on the second floor for premature infants and for those delivered by cesarean section, another unit of 20 bassinets on the same floor, and 2 other units on the third floor, each having 8 bassinets. Nursery personnel rotated through all the units but did not contribute to postpartum care of the mothers. Observations were made weekly of cultures of specimens from nurseries, linens, and the milk laboratory where mixtures were prepared; no pathogenic organisms were found. All infants received the same care, including a daily bath with hexachlorophene detergent (pHisoHex®). Observations on the sick infants are shown in Table 1.

The first patient with Ritter's disease, D.H., was born June 1. Erythema developed on June 3, the day of discharge. His family had been having recurrent pyodermal infections for several months. The mother was free of apparent infection at the time of delivery. Unfortunately, we were unable to secure culture specimens from members of the family other than the patient. The only other skin infection at this time was in an infant born May 30; impetigo developed at home after discharge. These two patients were the only ones who were not from the large nursery and not from the second floor.

The first case was typical of 7 of the 8. Erythema first appeared about the mouth and then became general. Within twenty-four hours, general exfoliation of the epidermis began. This process continued for three or four days and then gradually subsided, leaving no residual lesions.

All patients in the hospital were given methicillin, either alone or with penicillin G, for from seven to ten days. Administration was intravenous during the first stages in order to avoid repeated intramuscular injections and to keep the handling of the infants to a minimum.

Generally the infants were not critically ill, but No. 8, M.R., was extremely ill. He was born June 27, was circumcised in the delivery room, and did well until the day of discharge, July 1. His mother noted erythema about the buttocks and abdomen. Spread was rapid, and exfoliation began the next day. On admission to Milwaukee Children's Hospital he was vigorous and not very ill. The next day he began to pass loose stools frequently, became distended, and had a rapid pulse. Stool cultures were negative for pathogens. On the fourth day in the hospital he began to have fever, apneic spells, and twitching. Serum calcium concentration at this point was 8.4 mg. per 100 ml. On the fifth day he was improved. He was given parenteral methicillin with penicillin G for thirteen days. Topical treat-

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TABLE 1

INFANTS WITH SKIN INFECTIONS DURING AN EPIDEMIC OF RITTER'S DISEASE IN A HOSPITAL IN 1963

Patient	*Date of birth*	*Where and when circumcised*	*Age at onset (days)*	*Nursery*	*Clinical disease*	*Culture*	*Therapy*
1. D.	5-30	Delivery room	Unknown	3rd floor, small	Impetigo	None	Unknown
2. D.H.	6-1	Delivery room	3	3rd floor, small	Ritter's	Staph. aureus 3C-71	Methicillin
3. C.	6-12	Delivery room	4	2nd floor, large	Ritter's	Staph. aureus 3C-71	Penicillin G
4. R.W.	6-16	Nursery; 3 days	9	2nd floor, large	Ritter's	Staph. aureus 3C-71	Methicillin
5. H.	6-21	Delivery room	3	2nd floor, large	Ritter's	None	Erythromycin (orally)
6. F.B.	6-25	Delivery room	3	2nd floor, large	Ritter's	Staph. aureus 3C-71	Methicillin
7. R.N.	6-26	Nursery; 2 days	6	2nd floor, large	Ritter's	Staph. aureus 3C-71	Methicillin
8. M.R.	6-27	Nursery; 2 days	6	2nd floor, large	Ritter's	Staph. aureus 3C-71	Methicillin and penicillin G
9. L.	6-27	Nursery; 2 days	Unknown	2nd floor, large	Impetigo	None	Unknown
10. P.	6-28	Delivery room	8	2nd floor, large	Ritter's	Staph. aureus 3C-71	Erythromycin (orally)

ment was simply baths twice daily with pHiso-Hex®. His condition at the end of treatment was good.

All the patients in this small epidemic survived. None had any septic sequellae or severe necrotizing lesions. Five of the 8 patients were hospitalized and were given intravenous methicillin; 1, M.R., also received penicillin G, as noted above. Three patients were not hospitalized; 1 was given injections of penicillin G, and the other 2 received oral erythromycin. Remission in the patients not kept in the hospital was as satisfactory as that in the babies hospitalized and given intravenous methicillin. The organism was sensitive to penicillin and to erythromycin.

Cultural studies were done in 7 of the 8 patients with characteristic Ritter's disease. In all instances, Staph. aureus, phage type 3C-71, was isolated and identified.

All the patients were male and all had been circumcised. Five, including the first 2 patients, who were from the small nursery on the third floor, had been circumcised in the delivery room.

When the third case of Ritter's disease appeared, the following changes and precautions were put into effect at the hospital: (1) The large second-floor nursery from which all but 1 patient with Reitter's disease (D.H.) came was closed. It was then scrubbed completely and painted, and Formica tops were installed on all tables surfaces. (2) The rooms of the mothers with infants in the large nursery were closed and, before being reopened, washed thoroughly. (3) Circumcisions, which had routinely been done in the delivery room or at 48 hours of age by house staff or attending physicians in a different room for each floor, were postponed until the day of discharge for six weeks. (4) For two months all babies were examined by the attending physician just before discharge. (5) Cultural specimens from all nursery personnel were secured at one time and all cultures positive for Staph. aureus were sent to the Wisconsin State Laboratory of Hygiene for phage typing.

One student nurse was harboring Staph. aureus 3C-71 but was not working in the nursery when the reports became available; repeat cultures were negative. A practical nurse with Staph. aureus 71 in her nasopharynx was taken out of the nursery; repeat cultures were negative. After these procedures were completed, no new cases appeared. In 1 infant impetigo occurred three or four days after discharge, but cultural studies were not done; this case is not tabulated. The large nursery was reopened after six weeks.

REVIEW OF HOSPITAL RECORDS

A search of the files at Milwaukee Children's Hospital showed that 25 patients with Ritter's disease had been admitted during 1940-64. The data on these patients are summarized in Table 2. Included (Nos. 17-21) are the 5 patients (Nos. 2, 4, 6, 7, and 8 in Table 1) from the local epidemic who were admitted to the hospital.

Whenever cultures were made before any antibacterial treatment, Staph. aureus was invariably isolated. In patient No. 7 autopsy cultures showed Esch. coli in tissues of all regions except the nasopharynx, where Staph. aureus was found. In patient No. 22 Pseudomonas was cultured from the skin, but she had received penicillin before admission. In patient No. 23, from whom Staph. aureus, phage type 80-81, was isolated, impetigo was associated with general exfoliation, the only such occurrence in this group. The other instances from our files did not occur during epidemics, although the patients admitted in 1961, Nos. 13 and 14, were delivered by the

TABLE 2

PATIENTS WITH RITTER'S DISEASE ADMITTED TO MILWAUKEE CHILDREN'S HOSPITAL DURING 1940-64

Patient	*Date of birth*	*Age in days at onset*	*Cultural data (skin cultures, unless otherwise noted)*	*Treatment*	*% eosinophils*	*Outcome and comments*
1. B.B.	6-28-40	17	Staph. aureus	Boric acid and sulfapyridine	0 × 3	Died; sepsis and no right kidney
2. J.P.*	12-25-40	11	None	Sulfonamide ointment and potassium permanganate dressings	5	
3. M.A.*	2-15-44	14	Candida albicans, Esch. coli, and Staph. aureus in blood and lungs	None	Not done	Died; pneumonia and situs inversus
4. J.B.	7-21-44	3	None	Potassium permanganate	8, 10, 5	
5. F.B.	12-18-47	7	None	Penicillin G and sulfonamide	17-34 × 5	
6. J.K.	3- 6-48	4	Unspecified mixed flora in throat	Penicillin G	1	Died; no autopsy
7. G.N.K.	11-13-48	27	Staph. aureus, in ears and throat; Esch. coli on skin and in stool	Penicillin G and sulfonamide	0	Died; gangrenous pneumonia and hemorrhagic enterocolitis
8. D.P.	10-10-55	5	None	Penicillin G and sulfonamide	2	Survived
9. J.K.	8-30-56	9	Staph. aureus	Streptomycin, penicillin G, erythromycin, and potassium permaganate dressings	6	Survived
10. D.D.	9- 3-56	4	Staph. aureus	Novobiocin (Albamycin®) and bacitracin-polymyxin-neomycin ointment (Neo-Polycin®), topically	6, 6	Survived
11. S.C.W.*	6- 7-57	7	None	Burow's solution and pHisoHex® topically	9	Survived
12. T.P.	9-24-58	1	None	Chloramphenicol	0	Died; Staph. aureus sepsis and vascular ring
13. D.C.	6-29-61	5	Staph. aureus 3A, 3B, 3C, 55, and 71	Methicillin and penicillin G	3, 1, 2, 6	Survived
14. M.S.	7-20-61	5	Staph. aureus 3C, 55, and 71	Methicillin and penicillin G	9	Survived
15. A.S.*	5-22-62	8	Staph. aureus	Bacitracin, topically	0, 2, 3	
16. R.M.	11-8 -62	11	Staph. aureus	Tetracycline, penicillin G, and methicillin	2, 5	Survived
17. D.H.†	6- 1-63	3	Staph. aureus 3C-71	Methicillin	2	Survived
18. R.W.†	6-16-63	9	Staph. aureus 3C-71	Methicillin	2, 10, 4	Survived
19. F.B.†	6-25-63	3	Staph. aureus 3C-71	Methicillin	7	Survived
20. M.R.†	6-27-63	5	Staph. aureus 3C-71	Methicillin	0	Survived
21. R.N.†	6-26-63	6	Staph. aureus 3C-71	Methicillin and penicillin G	9	Survived
22. B.T.*	6-28-63	16	Pseudomonas	Penicillin G	18, 16, 2	Survived
23. R.L.	1- 3-64	8	Staph. aureus 52, 80, 81, 6, 7, and 54	Methicillin	5, 27	Survived
24. A.C.	1- 9-64	4	Staph. aureus	Methicillin and penicillin G	8	Survived until age 2 months; aspiration, no autopsy
25. M.P.	8-23-64	10	Staph. aureus 3A, 3B, 3C, 55, and 71	Methicillin and penicillin G	3	Survived

*Female †Also shown in Table 1



Epidermal exfoliation and erythema of Ritter's disease in patient M.R. Purulent exudate is apparent on glans penis.



same physician at one hospital, and the admission history of patient No. 5 indicated that another infant in the nursery had similar lesions.

Five of the 25 patients died. Autopsies were performed on 4. Three had major anomalies: absence of a right kidney, situs inversus, and a vascular ring, respectively. In the fourth, whose illness had begun at 27 days, postmortem examination revealed necrotizing pneumonia and hemorrhagic enterocolitis. Of the 18 patients with Ritter's disease admitted to Milwaukee Children's Hospital after 1948 and the 3 other patients from the local epidemic, only 1 died. This infant had general Staph. aureus sepsis, a complication not observed in most of our patients.

All the patients in the epidemic group and all but 5 of the infants seen at Children's Hospital were male, for a male-female ratio of 4.6 to 1. What is the reason for this distribution? Since all the patients in the epidemic had been circumcised, usually within the first 48 hours, one might wonder if the circumcision wound could be an important portal of entry for the infection. That the epidemic ended when circumcision was postponed to the day of discharge might support this possibility, but other studies will be needed for confirmation.

Although commonly a disease of neonates, Ritter's disease occasionally occurs in older infants and children. Not included in this report are 6 essentially identical reactions in older children admitted to Milwaukee Children's Hospital in the past ten years.

In reviewing this material we have noted, as have others,[14] that eosinophilia is a common accompaniment of Ritter's disease and sometimes is a striking feature. In several instances the percentage of eosinophilic cells was from 10 to 27. Also notable is the fact that eosinophilia was not present in the babies who died or in M.R., the only seriously ill patient in the epidemic group.

DIFFERENTIAL DIAGNOSIS

Ritter's disease is so striking that confusion with other disorders is unlikely. As mentioned, the disease is characterized by an erythematous reaction that frequently but not always begins about the mouth. Massive exfoliation of the epidermis follows, usually within twenty-four hours. Nikolsky's sign is present, and staphylococci can be recovered from the lesions and from the nasopharynx with regularity. Aside from having this massive epidermal reaction, the infants are generally not seriously sick early in the course of the illness. The typical skin lesions are illustrated on page 234.

Other lesions may superficially resemble Ritter's disease. Bullous impetigo may have a common cause and resemble the more general reaction in Ritter's disease. The general exfoliation of Leiner's disease may be confused with that of Ritter's disease, but the epidermis is not lost in such massive plaques. Epidermolysis bullosa may be similar to Ritter's disease, but progress is usually not so rapid and the separation is between epidermis and dermis rather than between epidermal layers (keratolysis).

CONCLUSION

Our observations lend substantial support to the view that Staph. aureus of phage group 2 is etiologically associated with Ritter's disease. Early treatment with methicillin or other effective antibiotics has changed Ritter's disease from a very serious, almost ominous illness to one from which recovery can be prompt and general septic complications absent.

The authors wish to thank Dr. F. Kummer for his assistance in the translation of some of the original articles.

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Hereditary Nephritis and Deafness

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In recent years attention has been directed to a familial disease characterized by intermittent hematuria. In addition, nerve deafness and ocular defects have been observed in some families. Males have been more severely affected and have frequently demonstrated progressive renal disease. We have had an opportunity to make some observations of a family which appears to exhibit characteristics which would permit its inclusion in this group. The family relationships are shown in Figure 1.

CASE REPORTS

Case 1. An 11-year-old girl was admitted to Milwaukee Children's Hospital on Jan. 19, 1964, following the discovery of hematuria on a routine urine examination. There had been no symptoms of dysuria, frequency, apparent hematuria, "cloudy urine," urgency, flank pain, fatigue, or anorexia. Physical examination showed no significant abnormalities. Blood pressure was 100/60-70 on repeated observations. Hemoglobin was 12, hematocrit 36, and white blood count 5,150, with 44 segments, 45 lymphocytes, 1 monocyte, and 10 eosinophils. Erythrocyte sedimentation rate was 22. Repeated urinalyses showed 0 to 6 to 12 red cells and 3 to 15 white cells, but casts were not observed. On one specimen there was a trace of protein and on another specimen, 1+. Urine cultures on 2 occasions showed no growth. Blood urea nitrogen was 13, coagulation time was ten minutes, bleeding time was one minute, and pinworm slide was negative. Antistreptolysin-O titer was 833 on Jan. 22 and 166 on Jan. 25. Endogenous creatinine clearance was 71 liters per square meter of body surface per twenty-four hours, and serum creatinine was 0.8 mg. percent. Addis count was 12,320,000 red and 5,600,000 white cells per twelve hours. Serum electrophoresis was not remarkable. Urinary amino acid excretion was normal. An intravenous pyelogram and voiding cystourethrogram were not remarkable. An audiogram showed normal hearing sensitivity bilaterally. Her course in the hospital was uneventful and follow-up since then has continued to show intermittent hematuria.

Case 2. The 8-year-old sibling of case 1 was in good health except for 2 previous lower urinary tract infections in 1960 and 1962, which had been treated with antibiotics. Cultures following these courses of treatment were negative. Six days prior to admission, microscopic hematuria was noted on a routine urinalysis. Two days prior to admission, urinalysis again showed microscopic hematuria and she was admitted to Milwaukee Children's Hospital on Jan. 19, 1964. The only symptom was suprapubic and lower abdominal discomfort on wearing tight waisted clothes. Physical examination showed no significant abnormalities. Blood pressure was 100/60, hemoglobin 11.0, hematocrit 31, white count 3,000 with 56 segments, 1 band cell, 39 lymphocytes, 1 monocyte, and 3 eosinophils. Erythrocyte sedimentation rate was 19. Repeated urinalyses showed persistent hematuria varying from "rare" to "¼ packed per high-power field." There were 0 to 3 to 5 white cells. On one urinalysis, occasional red cell casts were seen. There was no proteinuria or glycosuria. Urine cultures showed no growth on 2 occasions. A throat culture grew Streptococcus pneumoniae, Streptococcus viridans and Neisseria. Blood urea nitrogen was 15. Coagulation time was eight minutes and bleeding time one minute. Initial antistreptolysin-O titer was 166 and repeat was 50. Endogenous creatinine clearance was 65 L. per square meter of body surface per twenty-four hours and serum creatinine 0.7 mg. percent. Addis count was 6,000,000 red cells, 0 casts, and 0 white cells per twelve hours. Serum electrophoresis was unremarkable. Urinary amino acid excretion was normal. An intravenous pyelogram and voiding cystourethrogram were not remarkable. An audiogram showed normal hearing sensitivity bilaterally. Her course in the hospital was uneventful and she was discharged on Jan. 25.

Case 3. The 42-year-old father of the patients described in cases 1 and 2 has had recurrent urinary tract symptoms since 1956, when he first experienced frequency, occurring about every 10 minutes. In addition, he had a burning sensation at the end of micturition and left flank pain which radiated down the left leg with motion. He also experienced fever and shaking chills. After one week of symptoms he sought medical attention and the physician found albuminuria.

He was treated with penicillin and the symptoms cleared in one week. In about six months, he had a recurrence of the same symptoms, except he suffered no pain radiating down the leg. He was again treated with antibiotics with subsidence of symptoms in less than one week. One year later, 1958, similar symptoms recurred and he was hospitalized. An intravenous pyelogram and cystoscopy were reportedly normal at that time. He was told he had "blood cells" in the urine at that time, in addition to albumin. Since then he has had at least 4 more periods of frequency and flank pain. He also complains of fatigue in the last year. He has had almost daily headaches for the last two years, which have been throbbing at times. These are not consistently relieved by rest or acetylsalicylic acid.

When the patient was 10 years old he had a draining ear following a left tympanic membrane incision. His

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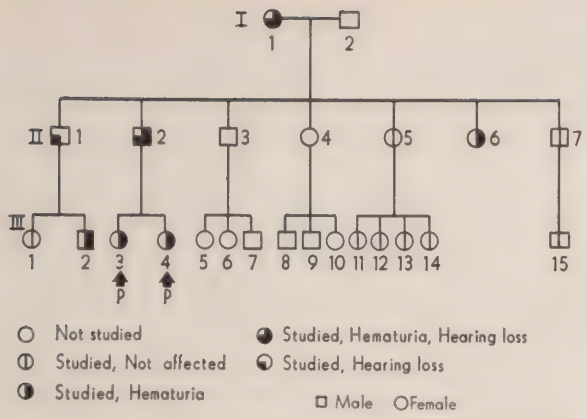


Fig. 1. Three generations of the H. family with hereditary nephritis and deafness.

hearing was checked four years ago and acuity was decreased. An audiogram (Fig. 2) showed for the right ear normal hearing sensitivity for speech range and a sensorineural loss in the high frequencies. There was mild sensorineural impairment for the left ear for the speech range and severe sensorineural component in high frequencies. Blood pressure was 140/85 right arm and 140/100 left arm. Urinalysis showed rare white cells, 8-70 red cells, no casts, pH 6 specific gravity 1.020, protein +, and no sugar or acetone. Addis count 19,380,000 red cells per twelve hours, with no casts or white cells.

Case 4 is the 39-year-old sister of case 3. She contracted polio in 1951, the residuals of which have required surgery on 2 occasions. On occasion, following an upper respiratory infection, she has noted some cloudy urine. Otherwise, she denies any urinary symptoms. She had had about 3 headaches per year for the past five years which are throbbing in character, are located behind the left eye, and are accompanied by nausea and vomiting, as well as photophobia. They are relieved by rectal suppositories. She has about 5 to 6 earaches per year, in association with upper respiratory infections, but she has never had purulent drainage. She denies any ocular symptoms. An audiogram showed normal hearing sensitivity, bilaterally with an acoustic notch at 4,000 cycles-per-second area.

Blood pressure was 110/80. Urinalysis showed no white cells, 12 to 15 red cells, 0 casts, pH 7, specific gravity 1.021, protein 0, no sugar or acetone. Addis count was 5,760,000 red cells, 0 casts, and 720,000 white cells per twelve hours. Endogenous creatinine clearance was 90 L. per square meter of body surface per twelve hours.

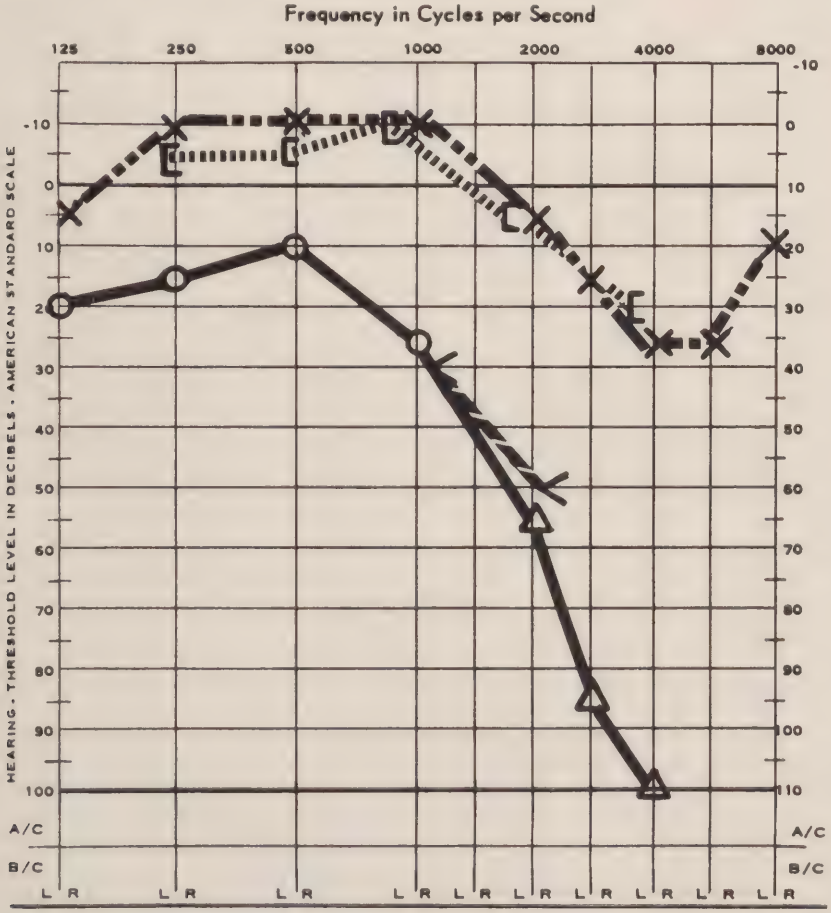


Fig. 2. Audiogram of case 3, showing sensorineural hearing loss for high frequencies on the right and loss in the speech range and high frequencies on the left.

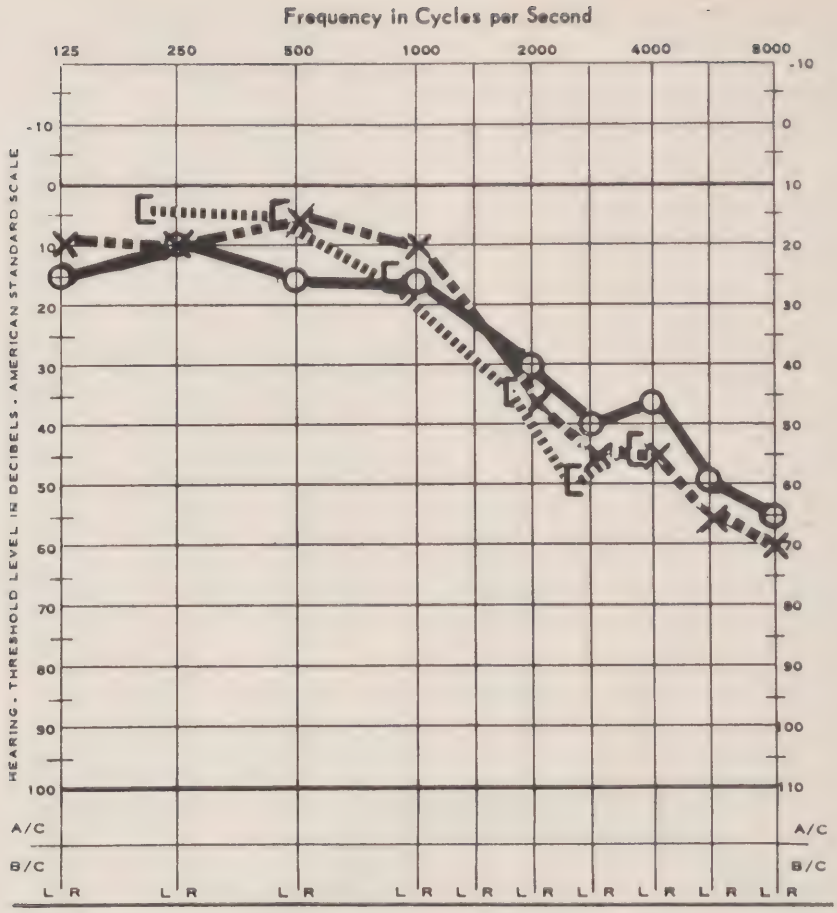


Fig. 3. Audiogram of case 4, showing mild bilateral sensorineural hearing impairment.

Serum creatinine was 0.6 mg. percent and blood urea nitrogen 13.

Case 5 is the 67-year-old mother of cases 3 and 4. The patient had a urinary infection with her third pregnancy. In recent years she has had burning and frequency and "cloudy urine" in association with upper respiratory infection. On at least one occasion, hematuria was found in association with these symptoms. For the last ten years she has had nocturia 2 times a night. An elevated blood pressure was noted in January 1964, and she is presently being treated for this. She complains of fatigue for the last one and one-half years and has had edema at night which is not present in the morning. There has been decreased hearing for the last 7 to 8 years and tinnitus for the last few months which has been intermittent. Diabetes was diagnosed a year ago, which is responding to diet and oral medication. An audiogram (Fig. 3) showed mild sensorineural hearing impairment bilaterally.

Blood pressure was 180/110. Urinalysis showed no white cells and 20 to 30 red cells, 0 casts, pH 6, specific gravity 1.014, protein 1+, and no sugar or acetone. Addis count was 10,815,000 red cells per twelve hours, with no casts or white cells. Endogenous creatinine clearance was 94.3 L. per square meter of body surface per twenty-four hours. Serum creatinine was 1.1 mg. percent and blood urea nitrogen 19.

DISCUSSION

Five of 15 members of the family we studied demonstrated hematuria and elevated Addis counts. Except for some dysuria or "cloudy" urine in association with upper respiratory tract infections, 4 of the 5 members have been asymptomatic. The fifth member, a male, has had urinary tract symptoms for eight years. Stultz and Burke listed 3 criteria for the diagnosis of familial hematuria: (1) F.H., of progressive renal disease in affected males, (2) presence or history of hematuria, which may be intermittent, and (3) nerve deafness in most of males and in some of females affected. The male member in the family who is affected is 42 years old, does not have an elevated blood urea nitrogen, and has never had symptoms of uremia. The majority of affected males have died earlier in life, frequently in their 20s, as indicated in previous reports, but Perkoff's study in 1958 included an autopsy report of a 44-year-old affected male. His series included a large number of descendants of the same family, (134 patients studied in first paper,

URINALYSIS

Patient	White cells	Red cells	Cast	pH	Specific gravity	Protein	Sugar	Acetone	BUN	Cretinine clearance L/24 hr/M²	Urine creatinine Mg. %	Serum creatinine Mg. %	Casts	Addis count WBC 10⁶/12 hr	Addis count RBC 10⁶/12 hr
I, 1 °	0	20-30	0	6	1.014	+	0	0	19	94.3	64	1.1	0	0	10.815
II, 1	0	0	0	6	1.032	0	0	0	23	85.3	180	1.2	0	.058	.058
II, 2 °	Rare	8-12	0	6	1.020	+	0	0	14	92.0	150	.8	0	0	19.380
II, 5	1-3	Occ.	0	6	1.026	0	0	0	15	105.4	162	.90	0	1.01	0
II, 6 °	Occ.	12-15	0	7.0	1.021	0	0	0	13	90	892	.6	0	.720	5.760
II, 7	0	Rare	0	7.0	1.015	0	0	0	8	81	144	1.0	0	0	0
III, 1	2-4	0-2	0	6	1.020	0	0	0	20	54.6	146	.75	0	.069	.023
III, 2	Occ.	Rare	0	6	1.028	0	0	0	13	108.0	65	.50	0	0	.031
III, 3 °	0 to 10-15	0 to 10-12	0	5 to 6	1.001 1.023	0 to 1+	0	0	11	71.0 87.0	128 87	0.8 .7	0	5.6	12.320
III, 4 °	0 to 3-5	Rare to ¼ pkd	Occ. RBC	5 to 7	1.012 1.025	0	0 to 1+	0	11	65 67	80 60	.7 .7	0	0	6.000
III, 11	—	—	—	—	—	—	—	—	11	—			—	—	—
III, 12	—	Solid	Amorph	5.5	1.028	0	0	0	12	89.7	280	.65	0	0	.462
III, 13	10-12	Rare	0	7.0	1.025	0	0	0	16	21.4	158	.65	0	1.2	0
III, 14	2-4	Occ.	0	6.5	1.025	0	0	0	17	26.3	104	.62	0	0	0
III, 15	0	0	0	5.0	1.021	0	0	0	12	83	56	.5	—	—	—

168 in second report). His 2 living males who were symptomatic at the time of the first writing had symptoms similar to our patient—pain in flank, easy fatigability, headache, and dysuria.

Audiograms were performed on 13 members of the family under discussion. They were tested for pure tone air and bone conduction sensitivity using the modified ascending threshold technique. A model 1,200 IAC (Industrial Acoustics Corporation) sound treated testing room and a Butane 15-C dual channel diagnostic audiometer with TDH-39 earphones and hearing aid type bone conduction receiver were used for testing. The only male member of the family with hematuria also showed hearing loss most severe in high frequencies. In Perkoff's second report of familial nephritis, of 86 audiograms performed, there were 20 males and 1 female who showed high tone deafness. Goldbloom, in his report, included an audiogram of one of the males affected. The hearing loss was 25 db. at 512 and increased to an average of 50 db. loss at 8,000 cycles. Sohar's[9] patients had a loss of about 40 db. at the 125 to 500 cycle range, and about 70 to 80 db. loss at the 1,000 to 8,000 cycle range. Our patient showed a similar pattern, with a loss of 35 db. at 1,000 cycles and maximum loss being 90 db. at 6,000 cycles (Fig. 2). A brother showed no urinary abnormalities, but has an abnormal audiogram with severe sensorineural loss for high frequencies (35 db. at 1,000 cycles, 110 db. at 4,000 cycles) in the right ear. None of the females studied, except for case 4, showed any hearing abnormality. Her audiogram (Fig. 3) would be compatible with the changes occurring with advancing age.

Despite the reports of this condition in recent years of families who fill the clinical criteria already listed, the pathogenesis of the renal lesions has not been definitely established. In Perkoff's initial study, postmortem findings of the kidneys of 2 involved members showed interstitial connective tissue infiltration as the most striking finding. In his later follow-up study, 5 percutaneous renal biopsies and 1 autopsy showed in one patient "foamy cells which resembled fat filled macrophages" and in the autopsy, material lipid, containing phagocytes interstitially. There were varying degrees of hyalinization of glomeruli in all biopsy specimens. The kidneys of the autopsied case were suggestive of chronic glomerulonephritis. The kidneys of the case discussed by Castleman demonstrated fat-filled cells which he felt were probably phagocytes. In addition, there were findings of glomerulonephritis. The 2 autopsied cases of Goldbloom showed small contracted kidneys with changes of chronic pyelonephritis. One of the 2 cases had fat-laden phagocytes. The necropsy findings, in the cases reported by Marin and Tyler, showed atrophic kidneys in 1, with fibrosis and dilated tubules. The other had contracted kidneys with findings of "chronic interstitial pyelonephritis." Both of these patients had neurological findings, and autopsy findings of nerves on the second patient showed, again, fat-filled macrophages. The authors raise the question of relation of fat-laden macrophages found in kidneys of previous reports to fat-filled macrophages of nerves of their cases. It is clear that pathological findings vary from pyelonephritis to glomerulonephritis. The possibility that the fat-laden macrophages may be one of the characteristics of this syndrome has not been clearly established.

Perkoff believes that familiaal hematuria is transmitted as a sex-linked dominant. He explains that if an affected male received the gene from his mother, it is carried on the X chromosome and thus would be transmitted to all his daughters. On the other hand, an affected male could not transmit the disease to his sons. An affected female could transmit the disease to either sons or daughters and half of each would be affected.

Our family, while small, is in agreement with Perkoff's conclusion. The grandmother of the propositus is known to have transmitted the disease to a son and a daughter. Only the son has offsprings and both his daughters are affected, as would be expected. In all probability, more carefully conducted family studies will reveal other unsuspected examples of this disease in instances of obscure hematuria.

Since there are no specific pathological changes or laboratory tests which enable us to establish the diagnosis of familial hematuria conclusively, we are left with the three criteria cited earlier by Burke and Sturtz of progress renal disease by history, hematuria, and nerve deafness, with males more severely affected.

SUMMARY

We have reported studies on a family, several members of which have shown hematuria and other evidence of renal disease in association with impairment of hearing, characterized by a loss in the higher ranges. These findings permit us to suggest that the family should be added to the families with hereditary nephritis previously described.

The authors are grateful to Dr. J. C. Peterson for suggestions made during the preparation of this report. The cooperation of Dr. Ahrens and laboratory personnel was much appreciated.

(Bibliography on page 246)

Studies in Histidinemia

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CRUCIAL TO PROGRESS in mental retardation is the identification of specific causes which are amenable to therapy. The example of phenylketonuria has encouraged biochemical research, and there is now good evidence that other inborn errors in the metabolism of amino acids are also associated with mental retardation. Genetic flaws in the catabolism of citrulline, homocystine, cystathionine, glycine, proline, hydroxyproline, lysine, argininosuccinic acid, and the branched amino acids have been recognized in mental defectives. These inborn errors of metabolism can be identified by amino acid chromatographic techniques applied to urine or blood or both. Only branched amino aciduria, sometimes called "Maple syrup urine disease," cystathioninuria, and phenylketonuria can be treated at present. The identification of the other amino acidurias is nevertheless important since the physician can provide precise genetic facts based on his knowledge that each of these diseases is inherited as a simple mendelian autosomal recessive characteristic. Although patients with these entities comprise but a small percentage of the total retardates, every family with such a child deserves to have him tested with the simple and inexpensive laboratory technique of amino acid chromatography.

When 10% ferric chloride is added to the urine of a patient with phenylketonuria, a transitory green color occurs because of the presence of phenylpyruvic acid. An unusual "false-positive" reaction was noted in a rare child who did not have phenylketonuria and who was not on medication. In these children, an excessive excretion of histidine in the urine and raised blood levels of this amino acid were demonstrated.

It was of interest that the first 6 patients with histidinemia, although described as "speech problems," were reported to have normal intelligence.[1–5] Recently, 2 patients with histidinemia and retardation have been described.[6,7] There are other unpublished cases associated with retardation.[8,9]

We shall describe a patient whom we have studied with histidinemia who is mentally retarded, has other congenital abnormalities, and had precocious onset of puberty. Some biochemical studies which indicate a few of the problems of this newly described entity will also be reported.

CASE HISTORY

J. P., a girl born May 2, 1954, was seen first at Milwaukee Children's Hospital at age 4 years, with the chief complaint of "cross eyes" for three and one-half years.

Family history. Father, age 46, has high blood pressure. Mother, age 36, and a brother, age 5, are living and well. There is no familial history of retardation or central nervous system disease.

Past history. Patient was born in Puerto Rico. Prenatal course was uncomplicated. Birth was normal and she weighed 6 lb. No abnormalities were noted in the neonatal period. She had recurrent upper respiratory infections, tonsillitis, and otitis media from age 4 months. Primary immunization against diphtheria, pertussis, and tetanus was received at age 6 months. She was tuberculin negative at age 4.

She sat alone at 1 year, walked at 2½ years, and was toilet trained and began to use words at 3½ years. At age 4 she was still fed infant foods.

A left internal squint was noted first at age 5 months and was treated with exercises; glasses were prescribed at 18 months without improvement. No impairment of vision or nystagmus was noted.

Physical examination was first performed on May 1, 1958. Her weight was 34½ lb. (twenty-fifth percentile). Her height was 39 in. (twenty-fifth percentile). She was hyperactive and performed at a developmental level below her chronologic age. Her teeth were small, incom-

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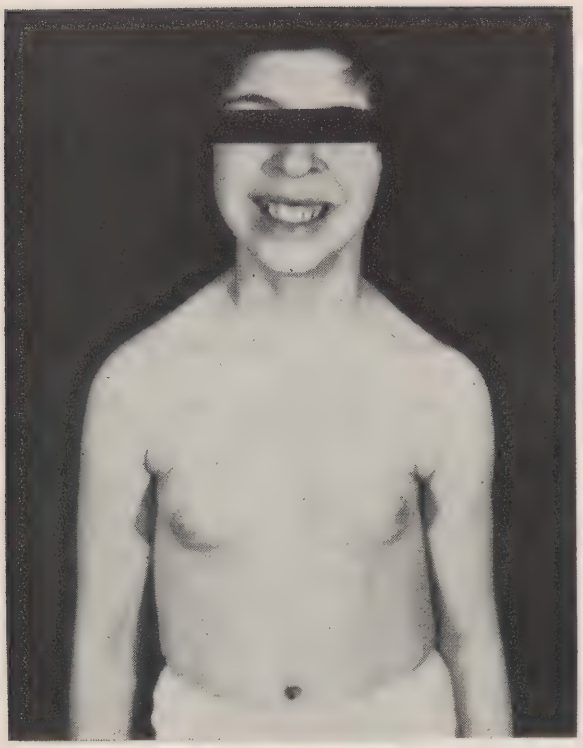


Fig. 1. Patient at 8 years

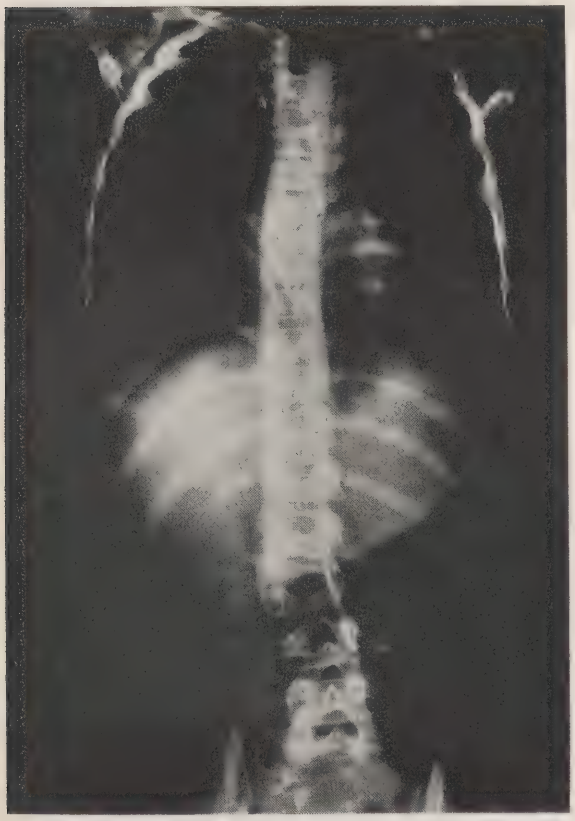


Fig. 2. X-ray which demonstrates hemivertebrae of lumbar spine

pletely covered with enamel, and widely spaced (Fig. 1). Her eyes were widely spaced, and a left internal strabismus was present. Her fifth finger curved in.

Laboratory studies revealed a white blood count of 13,350 with 26% segmented forms, 4 eosinophils, 2 basophils, 5 monocytes, and 63 lymphocytes. Hemoglobin was 12.5 gm. X-rays of the skull were normal. Bone age was between 3 years 3 months and 3 years 9 months. Kline test was negative. Urine was negative except for a positive ferric chloride reaction.

Psychological report excerpts at age 4: "Muscular coordination is poor for manipulative aspects. . . . Hyperactive, distractible, confused child with retarded language development, minimal perceptual efficiency and poor comprehension . . . . She wanders from object to object . . . . If some level or degree of deviation must be indicated, this little girl is functioning in the early stages of perceptual development at approximately an 18 month old level."

Course. From age 4 to 4½ the patient was seen often for respiratory tract infections. At age 4½ a bilateral medial recti recession was performed without incident. Following this surgical procedure she left Milwaukee and was not seen for two years.

When seen again at age 6½ years, bilaterally, easily displaceable patellae associated with genu valgum were noted. A right thoracic and left lumbar scoliosis were present, and the right leg was shorter than the left. X-rays revealed multiple congenital hemivertebrae with 14 thoracic, 6 lumbar segments, and 14 ribs (Fig. 2). Her height was 45½ in. (fiftieth percentile), and weight was 44 lb. (fiftieth percentile). She continued to have recurrent episodes of acute tonsillitis and otitis media. At age 6⅔ years a bilateral transfer of the semitendinosi tendons to the patellae was performed, and she was placed in casts. This procedure failed to stabilize her knees, and the patellae soon began to dislocate again.

Because of recurrent otitis and her speech difficulty, an audiogram was performed at age 7 and was essentially normal. An uneventful tonsillectomy and adenoidectomy were then performed. Another audiometric evaluation at age 8 was also normal.

At age 7 years, 3 months, she was admitted because of fever and pain in her right knee. Within a week her temperature gradually became normal, and no cause was established for this illness.

In September 1961 psychological testing revealed the following:

Binet, Form L.M.: C.A. 7-2, M.A. 4-3, I.Q. 56
Peabody Picture Vocabulary Test: C.A. 7-2, M.A. 4-1, I.Q. 66.

In January 1962, at age 7½ years, breast enlargement was noted. Examination revealed definite pigmentation of both breasts and palpable glandular tissue. There was generalized hirsutism and pubic but no axillary hair. The clitoris was slightly enlarged. A small mass consistent with an immature uterus was palpable per rectum. Twenty-four-hour urine for 17-ketosteroids was 1.8 mg. Follicle-stimulating hormone was under 6 mouse uterine units per twenty-four hours. A vaginal smear revealed 100% cornified epithelial cells.

In December 1962, at age 8 years, 8 months, the following psychometric test was reported:

Standard Binet: M.A. 5-3, I.Q. 58
Van Alstine Picture Vocabulary: M.A. 5-11, I.Q. 68
Columbia Mental Maturity Scale: M.A. 5-5, I.Q. 62

At age 9 years, 8 months, her height was 55½ in. (seventy-fifth percentile) and her weight was 74½ lb. (seventy-fifth percentile).

LABORATORY INVESTIGATIONS

Urine and amino acids. Extraction with Dowex 50W resins was followed by elution with ammonia and 2-dimensional chromatographic analysis on Whatman No. 1 in butanol: acetic acid: water (4:1:5), and secondary butanol: tertiary butanol: methyl ethyl ketone: water (4:4:8:5), with 1 cc. of diethylamine. Ninhydrin was the developing reagent.

Quantitative analysis for histidine was performed by Dr. Charles Altshuler, St. Joseph's Hospital, Milwaukee, Wisconsin. The bacterial decarboxylase method of Soupart[10] was employed.

Quantitative amino acid analysis[11] was performed on the Moore and Stein apparatus by Dr. Leon E. Rosenberg of the National Institute of Health.

Imidazoles. These were extracted, eluted, and chromatographed in the first dimension with the method described above for amino acids. The developing spray was Pauly's reagent. Two-dimensional chromatograms were also run with butanol: pyridine: water (1:1:1) as the additional solvent.

Neat urine was also applied to Whatman No. 1, run in butanol: acetic acid: water (4:1:5) overnight, dried, and sprayed with 10% ferric chloride.

Quantitative imidazole pyruvic acid was performed according to the method of La Du.[5]

Cerebrospinal fluid. This material was analyzed for amino acids in a manner identical to that described above for urine.

Blood. Phenylalanine was originally determined in the Rosner-Hixson Laboratories, Chicago, Illinois. The microbiological method was employed.[10]

Plasma histidine levels were determined using La Du's[5] modification of his own method for phenylalanine. Dr. La Du kindly performed the initial level in his laboratory at the National Institute of Health. Later levels were run in our own laboratories.

Histidine tolerance test. L-histidine, 0.1 gm. per kilogram of body weight, dissolved in orange juice, was given after an overnight fast. Blood was drawn at one, two, three, five, and twelve hours.

Urine was examined before and during the tolerance test for amino acids and imidazoles and with the ferric chloride reagent.

RESULTS

Urine. Many random urine samples gave a positive ferric chloride test. The color often was gray-black and persisted. This was quite different from the transitory green reaction in the phenylketonuric. The intensity of this reaction was variable.

Two-dimensional urinary amino acid analysis revealed only a marked excretion of histidine. This was confirmed by the bacterial decarboxylase method. A total urinary volume of 660 cc. contained 709 mg. of histidine and 0.55 gm. of creatinine. This is a markedly elevated amount of histidine, 1,276 mg. per gram of creatinine. The patient's mother, for example, excreted 174.5 mg. of histidine per gram of urinary creatinine.

The results of the urinary amino acids by the method of Moore and Stein are given in the table and demonstrated the histidinuria. Other amino acids were normal.

Imidazole chromatography revealed the presence of imidazole acetic and imidazole lactic acids. An unidentified Pauly spot was also present. This did not react with ferric chloride, and we do not believe it was imidazole pyruvic acid.

Urine to which 2,4-dinitrophenylhydrazine was added did not give a precipitate immediately but a fine sediment formed overnight in the cold.

Blood. Blood phenylalanine determination was normal, 1.64 mg. per 100 ml. Plasma histidine was initially 15 mg. per 100 ml. as performed by Dr. La Du; normal plasma histidine is between 1 and 3 mg. per 100 ml. The patient was then placed on a low animal protein diet. We asked her mother to omit fish, meat, eggs, and cheese. After three months on this regimen her blood histidine level was 9 mg. per 100 ml. After four months it was 7 mg. per 100 ml. No improvement

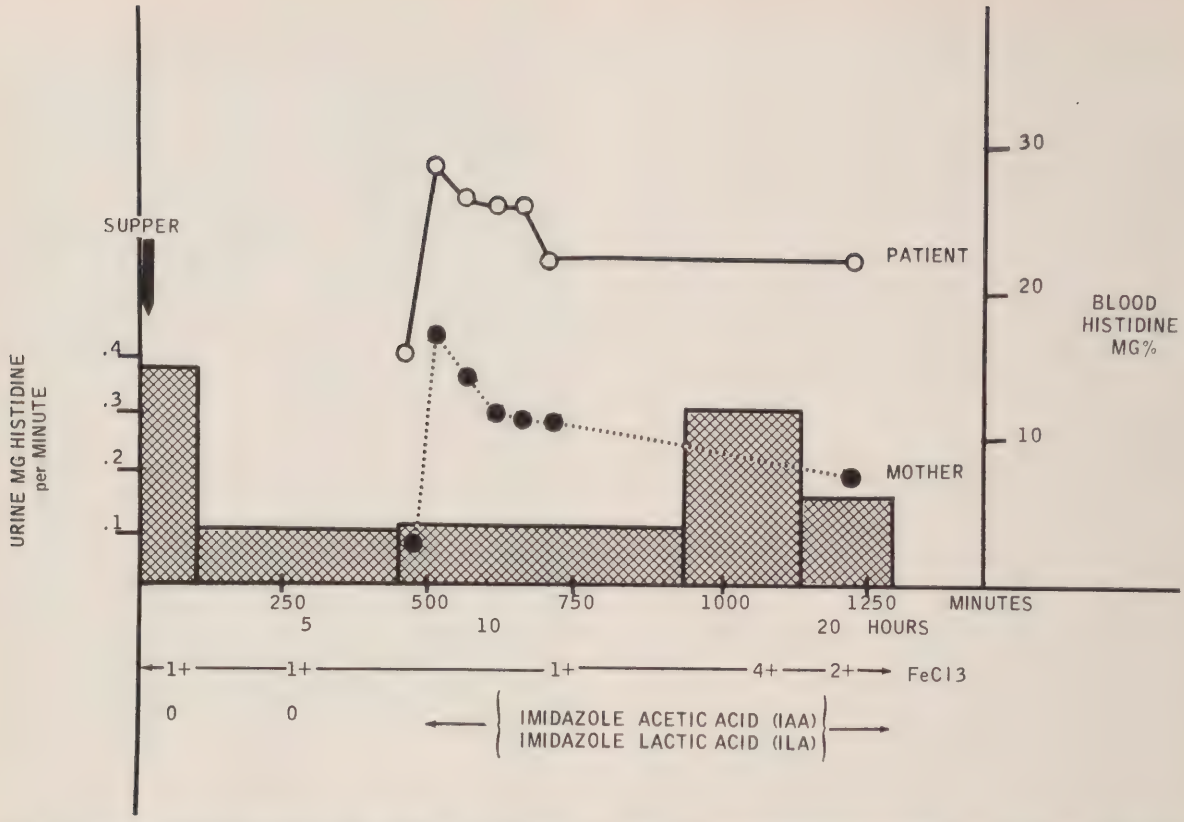


Fig. 3. Histidine tolerance test. The ingestion of histidine followed drawing of fasting blood level at seven and one-half hours. For details see text under Methods. Note difference in blood levels of patient and her mother. The cross-hatched area indicates urinary excretion of histidine by patient. The ferric chloride reaction and imidazole excretion also refer to patient.

in her intellectual function was discernible with psychological testing. Her urinary ferric chloride reaction was then essentially negative, and only a slight trace of imidazole lactic acid was present.

Ten days after these results were obtained the patient ate a full Thanksgiving dinner. A urine test soon after was not positive with ferric chloride, and there was a marked amount of histidine and imidazole acetic and lactic acids present. She was allowed a regular diet, and two months later her blood histidine level was 11 mg. per 100 ml.

HISTIDINE TOLERANCE

The histidine tolerance curve is depicted in figure 3. For comparison, the tolerance of the patient's mother is also indicated. The figure graphically illustrates the patient's urinary excretion of ferric chloride–positive material, imidazoles, and histidine before and during the histidine tolerance. The ingestion of histidine increased the urinary excretion of imidazole pyruvic acid, and a weakly positive ferric chloride reaction became strongly positive. During this same period there was an increase in the urinary excretion of imidazole acetic and imidazole lactic acids. Not indicated in the graph is the fact that the patient's mother also excreted imidazole acetic and lactic acids during her histidine tolerance. Unlike her daughter, however, she never excreted any urinary ferric chloride-positive material.

DISCUSSION

Most of our observations confirm findings which have already been demonstrated by others. Some points deserve emphasis.

It was earlier inferred from loading studies with urocanic acid that the block in histidinemia is at histidase, the enzyme which catalyzes the conversion of histidine to urocanic acid. The validity of this hypothesis was established by La Du's[4] demonstration of the absence of histidase in skin. We have previously reported studies in this patient with C^{14}-histidine[12] which implicate histidase deficiency as the cause of this disease, and we have confirmed reports that the positive ferric chloride material was imidazole pyruvic acid. The increased excretion of imid-

MILLIGRAMS PER TWENTY-FOUR HOURS

Amino acid	*Patient-J.P.*	*Normal*
Taurine	41.73	86-294
Methionine	21.40	15- 53
Serine	32.10	27- 73
Asparagine-glutamine	39.59	34- 92
Glutamic acid	1.60	10
Glycine	34.24	68-199
Alanine	22.47	21- 71
Valine	3.21	10
Tyrosine	8.02	15- 49
Phenylalanine	6.42	9- 31
Beta-amino-iso-butyric acid	7.49	0-252
Ornithine	1.60	0-252
Ethanolamine	9.10	
Lysine	11.24	7- 48
1-methyl histidine	42.80	20-150
Histidine	514.67	113-320
3-methyl histidine	17.12	20-150
Creatinine	276.60	

azole acetic acid and lactic acid also follows from such an enzymatic defect. These pathways are indicated in figure 4 and are very similar to those in phenylketonuria.

The ferric chloride test appears to vary with the intake of protein. This was also noted by Ghadimi.[2] Davies' and Robinson's[6] patient excreted imidazole pyruvic acid only during a histidine tolerance test. Our experience with urinary amino acid paper chromatographic analysis elicits the observation that it is easy to overlook increased urinary amounts of histidine. We have pointed out that chromatographic tests for other imidazoles are only weakly positive when the patient is on a low-protein diet. This prompts the speculation that other cases of this disease might be overlooked.

It is difficult to evaluate the clinical manifestations of a disease known to affect but 8 reported patients. Recurrent infections have been part of 2 other clinical histories.[4,6] Growth retardation has occurred twice.[1,6] Two patients have had tremors,[2,6] and 1 has had ataxia.[2,5] Other congenital abnormalities have not been reported except for bilateral inguinal hernias and spinal malformations in one of La Du's[4] patients. The latter are of interest when compared to our patient.

Mental retardation must now be considered as a manifestation of this disease, since 3 of the published 8 patients and most of the 11 unpublished patients[8,9] have had this unfortunate symptom. Many of the patients with histidinemia who are said not to be retarded are described as having "speech problems." The cause of the vari-

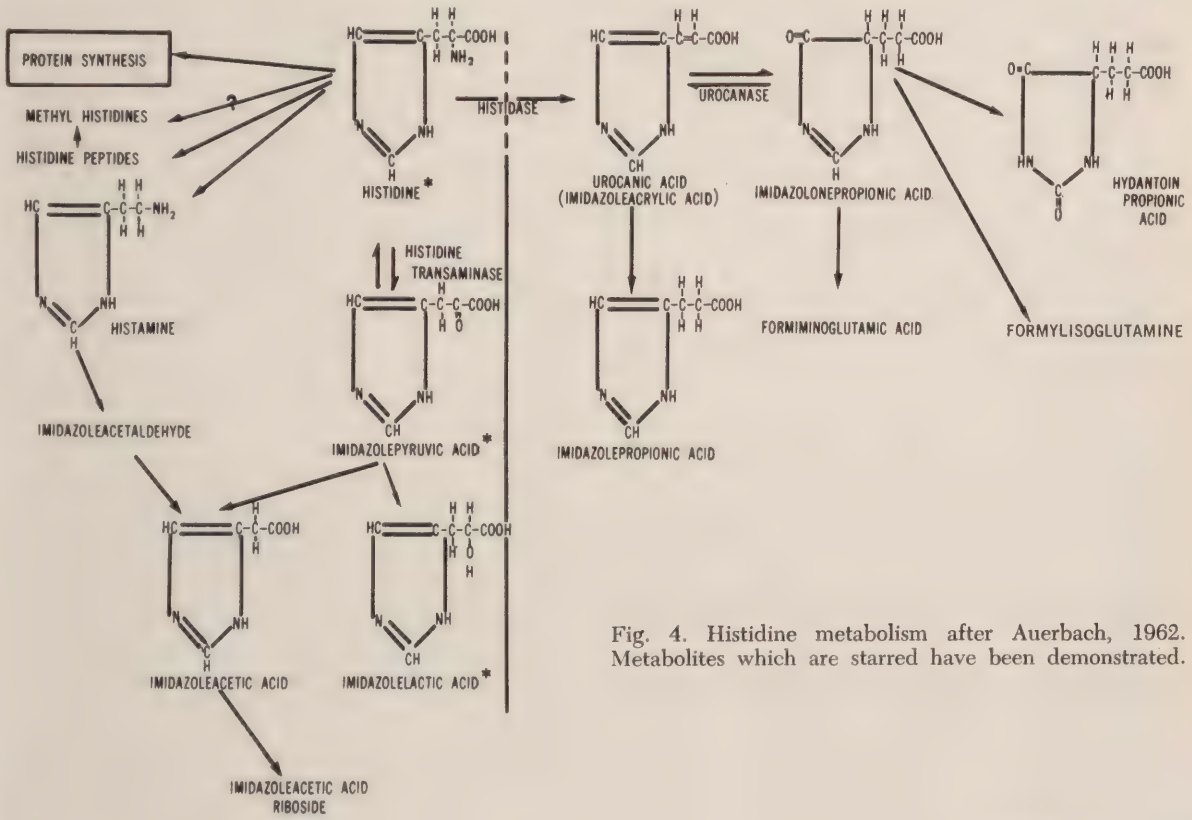


Fig. 4. Histidine metabolism after Auerbach, 1962. Metabolites which are starred have been demonstrated.

ability in the central nervous system manifestations of this disease is a fascinating question which warrants further investigation.

The value of a low histidine diet in histidinemia is unknown. Histidine is an "essential" amino acid only during childhood. If the chromatographic screening procedure described for blood by Efron and associates[13] could be employed as a routine, histidinemia might be diagnosed in the newborn period. The possibility would then exist of testing the value of a low histidine diet in histidinemia.

SUMMARY

We have emphasized the value of chromatographic techniques in the search for disorders in the metabolism of amino acids which are associated with developmental retardation. The case history and biochemical findings of a child with histidinemia have been presented as an example. Contrary to the original reports, this disease is often associated with mental retardation. Patients with histidinemia excrete imidazole pyruvic acid in their urine, and it is this material which is responsible for the ferric chloride reaction. Since imidazole pyruvic acid is not always present, and probably reflects the amount of protein in the patient's diet, the ferric chloride reaction is variable. The diagnosis and differentiation from phenylketonuria can best be accomplished by demonstrating an elevated serum concentration of histidine. The blood phenylalanine level, in contrast to the value in the patient with phenylketonuria, is normal. Finally, we have speculated that if the diagnosis can be made in infancy, when histidine is an essential amino acid, a therapeutic trial of a diet low in histidine could be evaluated.

Dr. Stanley Berlow was supported by Public Health Service Research Career Program Award 5K3-HD-14,942-02.

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HEREDITARY NEPHRITIS AND DEAFNESS

(Continued from page 240)

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Foreign Bodies in the Alimentary Tract of Infants and Children

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CHILDREN WILL TRY to swallow anything that fits into their mouths. Most foreign bodies pass readily into the stomach and negotiate the remainder of the gastrointestinal tract without difficulty; nevertheless, the experience frequently is traumatic for the patient, the parents, and the physician, all of whom apprehensively await the removal or the ultimate passage of the foreign body.[1]

The purpose of this paper is to report 455 instances of foreign bodies in the alimentary tract in patients admitted to Milwaukee Children's Hospital during the past forty years, and to identify the types of foreign bodies that may give difficulty in diagnosis and care (Tables 1-5). The outpatient department of Milwaukee Children's Hospital has followed and cared for approximately 3 to 4 times this number of patients with ingested foreign bodies. In the past few years only those requiring endoscopy or those where difficulty was anticipated were hospitalized.

Symptoms. The initial symptoms of choking, gagging, coughing, and wheezing may be followed by a symptomless interval after the ingestion of a foreign body. This interval should not preclude adequate study to exclude the possibility of a foreign body because of the potentially disasterous sequelae. Although in some cases symptoms may disappear after the initial episode, others may manifest aphagia, dysphagia, or drooling.

Diagnosis. Properly performed radiographic studies are a great aid in the recognition of alimentary tract foreign bodies; but if negative, endoscopy based on clinical findings may be required.

Since poorly performed radiographic studies are the cause of more diagnostic errors than any other single factor, a definite procedure is essential.[2] Adequate initial X-rays consist of a lateral film of the neck to include the area from the roof of the nasal cavity to the lower neck and an anteroposterior film from the neck to the anus; uncertainty necessitates repeating the films (Fig. 1). The uncooperative patient whose movements could obscure the foreign body requires filming with exposures of one-sixtieth to one-twentieth of a second. The patient must be completely stripped with no protective padding or sheeting between him and the X-ray table. Objects interposed inadvertently between the patient and the film as well as faulty cassettes, intensifying screens, film processing, objects on patients, and calcified lymph nodes are sources of false-positive diagnosis. An additional lateral chest or abdominal film may determine the exact location and configuration of the foreign body. Multiple foreign bodies may be present and superimposed on a single view but readily identified on anteroposterior and lateral projections (Fig. 2).

The density of the foreign body dictates the proper radiologic studies. If the type of foreign body suspected of being ingested is known, a duplicate should be obtained, particularly in instances of glass and plastic materials, so that the opacity may be determined by placing the duplicate on the abdomen or thigh and making an additional radiograph. Foreign bodies vary from the markedly opaque metallic objects to hyperlucent substances such as a mass of fat or gas bubbles associated with infection adjacent to a foreign body. The dense and radiolucent foreign body can be recognized with plain films. Those objects whose density is similar to the soft tissues require fluoroscopy with opaque contrast media (Fig. 3).

Fluoroscopy with image amplification provides better visualization and a significant reduction in radiation through conventional fluoroscopy. Water soluble opaques such as methylglucamine diatrizoate (Gastrografin®) are less likely to ob-

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TABLE 1

COINS, BUTTONS, DISKS, RINGS, WASHERS

Type of foreign body	*Total*	*Removed with esophagoscope*	*Passed through stomach*	*Average time to pass*	*Average age*	
Pennies	108	98	12	2 days	2 to 2½	
Nickels	46	39	8	3 days	2 to 2½	One removed surgically five months after swallowing. 1951.
Dimes	5	5	0	0 days	2 to 2½	
Quarters	20	18	2	3 days	2½ to 6	
Half-dollars	1	1			8	
Buttons	16	12	3	2 days	3½	One removed with esophagoscope, died of pneumonia, 1929.
Whistles	7	5	2	1 day	5½	
Disks	20	15	3	4 days	3	One died of bronchopneumonia, 1924.
Bullets	1	0	1	4 days	6	
Marbles	5	2	1		3½	
Ring	3	2	1	4 days	5	
Key	3	3	0	0 days	5 22 months	
Total	234	200	33	3 days	3 years	

TABLE 2

SAFETY PINS

Type of foreign body	*Total*	*Removed with esophagoscope*	*Average time to pass*	*Average age*	*Surgery*
Open pins (large)	50	24	4½ days	2½	1. Operated ten days later. Pin in stomach. 2. Operated ten days later. Pin in Meckel's. 3. Operated. Couldn't find pin. Passed seven days later. 4. Pushed into stomach. Lodged in duodenum. Removed three days later.
Open pins (small)	10	2	3 days	1	1. Operated one month later. Pin in stomach.
Closed pins	4	0	7 to 10 days	5½ to 6	
Total	64	26	5 days	2	

TABLE 3

OBJECTS WITH ONE SHARP POINT

Type of foreign body	*Total*	*Removed with esophagoscope*	*Average time to pass*	*Average age*	
Straight pins	21	1	3 days	4½	
Nails	6	1	3 days	1½	One developed a lung abscess after esophagoscopy.
Tacks	10	7	3 days	1	One tack caught at site of previous tracheo-esophageal repair.
Ornamental pins and badge pins	10	5	2½ days	6	One died of pneumonia, 1946. One operated twelve days later. Pin found in stomach.
Bobby pins	11	0	7 days	2 to 3	Five cases required surgery. One perforated duodenum.
Total	58	14	3 days		

TABLE 4

OBJECTS WITH MULTIPLE POINTS

Type of foreign body	*Total*	*Removed with esophagoscope*	*Average time to pass*	*Average age*	
Sewing needles	3	0	0	4	All cases required operation. 1. Found penetrating and lodged in stomach wall. 2. Found penetrating and lodged in duodenal wall. 3. Found outside the intestinal lumen in a ball of omentum.
Glass	7	0	3 days	1½	Two perforated the esophagus and caused mediastinitis.
Metal star and triangle	10	7	6 days	4	Star removed with esophagoscope.
Wire	2	1	0	3½	1. Admitted for appendectomy. Wire found in mass in ascending colon. 2. Removed with esophagoscope, 1928. Punctured lung and died.
Bone	7	5	6 days	5	
Jacks	10	9	5 days	4	One pushed into stomach with esophagoscope. Passed without difficulty.
Treble fishhook	1	1	0	3 months	
Total	40	23			

TABLE 5

SUMMARY OF FOREIGN BODIES IN THE GASTROINTESTINAL TRACT IN INFANTS AND CHILDREN

Type of foreign body	*Total*	*Removed with esophagoscope*	*Requiring surgery*	*Average time to pass*	*Mortality*
Coins, buttons, disks, rings, and washers	234	200 (85%)	1 (½%)	3 days	2 (1%)
Safety pins	64	26 (40%)	5 (8%)	5 days	0
One sharp point, such as nails, tacks, straight pins, badge pins, and bobby pins	58	14 (24%)	6 (10%)	3 days	1 (2%)
Multiple sharp points, such as glass, sewing needles, wire, and metal triangles	40	23 (57%)	4 (10%)	5 days	1 (2½%)
Miscellaneous	59	38 (65%)	1 (1½%)		0
Total	455	301 (66%)	17 (3½%)		

scure normal anatomy and the foreign body for the endoscopist. A negative shadow surrounded by the opaque will be noted. Sharp objects may be fixed to the gut wall while smooth ones move about in the gut. The point of a sharp object penetrating the gut wall will be obvious (Fig. 4). Occasionally, barium paste mixed with cotton may catch on a sharp foreign body and identify its location when other methods fail. In those instances where a cooperative patient identifies the level of the foreign body in the esophagus but it cannot be demonstrated by water soluble opaques, this type of contrast study may be diagnostic. Flat esophageal foreign bodies such as coins lie with their greatest diameter in the coronal plane in nearly all instances; in the larynx or trachea the greatest diameter of a flat foreign body is usually in the sagittal plane. The likely points of arrest of the foreign body in the esophagus are at the level of the cricoid, aortic arch, and just above the diaphragmatic hiatus. Ingested wax crayon may be identified in the stomach because of surrounding air or by the use of contrast media.[3] Yellow or orange wax crayons particularly may contain paranitraniline. This chemical may produce intense methemoglobinemia with resultant cyanosis, coma, and possibly death.

Treatment. Foreign bodies lodging in the esophagus constitute emergencies and require immediate hospitalization and esophagoscopy. Sixty-six percent of our patients required esophagoscopy. Most objects are removed during this procedure, especially open safety pins, while





Fig. 1. (A) Negative anteroposterior film. (B) Same patient. Open safety pin in nasopharynx visible only on lateral view of neck and face.

round and smooth objects may be pushed into the stomach if they cannot be easily grasped and removed. Occasionally a sharp object may perforate the esophagus which occurred in two of our patients when pieces of glass perforated the esophagus and caused mediastinitis.[4] A bolus of meat impacted in the esophagus may be softened by the introduction of 5 cc. of 5% solution of papain every fifteen or twenty minutes for a period of several hours.

If a foreign body can pass the esophagogastric junction into the stomach, it will usually pass the pylorus; however, surgical removal was done in about 10% of instances where the foreign bodies, primarily open safety pins or other objects with one or several sharp points, were in the stomach. It should be emphasized that if the object in the stomach is composed of lead, removal must be seriously considered because if it remains in the stomach longer than a few weeks, lead poisoning may result.[5]

A reasonable rule to follow is that if a foreign body remains in one location for longer than four or five days, surgical removal should be considered, especially if any symptomatology occurs. As long as the foreign body continues to move through the intestinal tract the patient is usually not in danger. In only one case was it necessary to remove a round object from the stomach. This was a nickel that was watched for five months and then removed primarily because of insistence

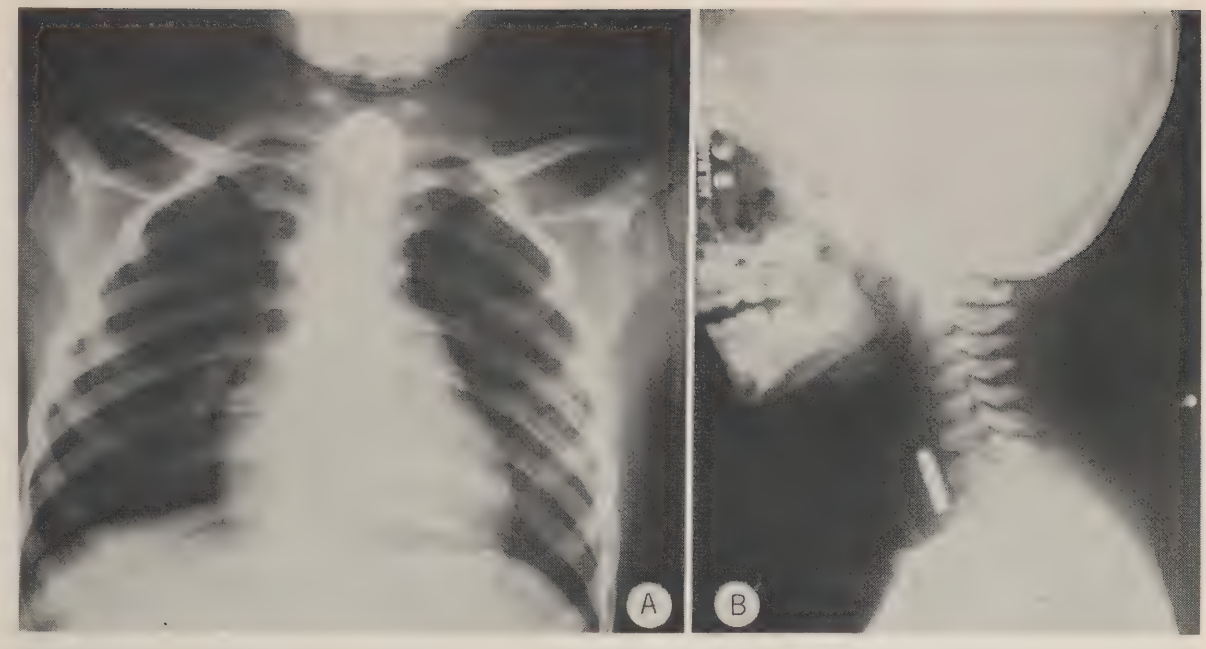
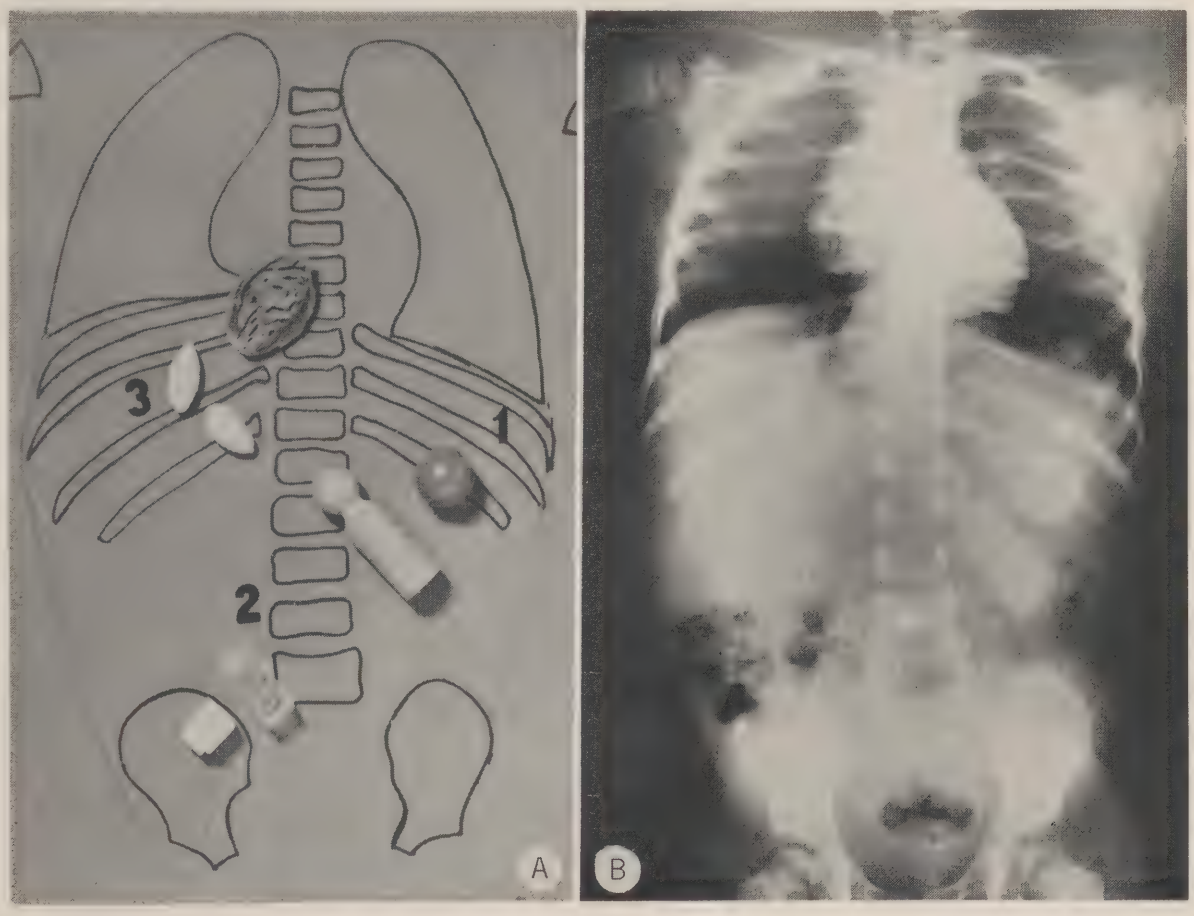


Fig. 2. (A) Coin in upper esophagus. (B) Same patient. Two coins noted on lateral view of face and neck.

Fig. 3. (A) Line drawing of position and density of various objects seen in Fig. 3B. (B) Differential opacity of objects placed on abdomen and X-rayed from Fig. 3A.



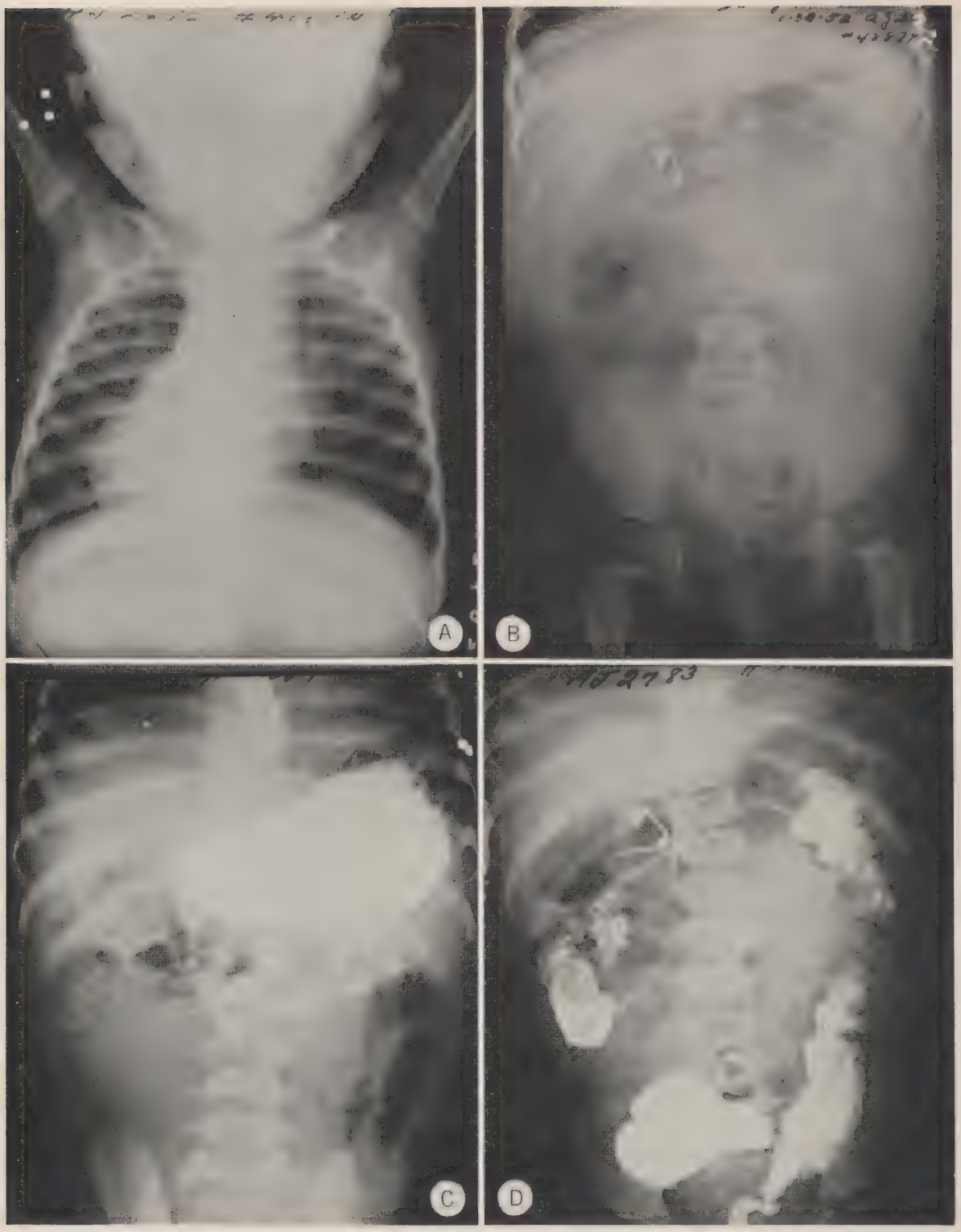


Fig. 4. (A) Open safety pin in upper esophagus on admission. (B) Position of open safety pin after passage into the stomach, pushed into stomach by esophagoscopist the same day. (C) Point of safety pin penetrating wall of duodenum two days after Fig. 4B. (D) No change in position of safety pin two days after 4C, removed surgically with recovery.

from the family. The length of the foreign body is of considerable importance, particularly in relation to bobby pins, nails, pencils, and needles. A foreign body longer than 5 cm. in a child under 2 years old may have considerable difficulty passing the duodenal loop into the jejunum. In infants foreign bodies 2 or 3 cm. in length may also become impacted in the duodenum.

The use of an "on-off" alnico magnet recently described by Luborsky and associates is an excellent instrument for the removal of magnetic foreign bodies from the stomach.[6] Nonopaque foreign bodies in the appendix, Meckel's diverticulum, or in narrowed areas of the small and large bowel usually are not recognizable by plain X-ray studies and only occasionally by contrast studies unless evidence of obstruction is noted. Foreign bodies distal to the sigmoid are best diagnosed and treated by endoscopy and digital means. Contrast X-ray studies after the removal of foreign bodies should be performed because of the possibility of an intrinsic organic lesion predisposing to the arrestment of the foreign body.

Mortality. All 4 deaths in this series were due to respiratory complications with the last death occurring in 1946.

CONCLUSIONS

1. Children will swallow foreign bodies, many of which will pass into the stomach and through the remainder of the alimentary tract without difficulty.

2. Immediate hospitalization and esophagoscopy are required for foreign bodies lodging proximal to the diaphragmatic hiatus.

3. Children with unexplained symptoms of choking, gagging, coughing, or wheezing need properly performed radiologic studies to rule out a foreign body.

4. Cathartics, special bulk diets, or such innovations as the "cotton sandwich" should not be used to hasten the movement of the foreign body through the intestinal tract.

5. Poor radiographic studies are the cause of more errors in diagnosis than any other single factor.

6. Close observation, preferably with hospitalization, is urged for children with open safety pins or other elongated sharp objects in the intestinal tract.

7. The surgeon should not be in a hurry to remove an asymptomatic foreign body. This is particularly true if it continues to move through the gastrointestinal tract, provided that it does not remain in one location longer than four or five days when lying distal to the pylorus.

8. If surgical removal is contemplated, X-ray study immediately prior to surgery is necessary to accurately locate the object.

9. For medicolegal protection a final radiographic study is advisable to show that the foreign body has been removed or has passed and to obviate the possibility of leaving a second unrecognized foreign body. Contrast studies may result in identification of an organic narrowing which precipitated the arrestment of the foreign body.

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Thymic Alymphoplasia with Pancreatic Fibrosis and Mucoviscidosis

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THYMIC ALYMPHOPLASIA, a developmental anomaly of the thymus characterized by the absence of small lymphocytes and Hassall's corpuscles, has been found in infants and children with agammaglobulinemia and lymphopenia,[1] and has also been found with congenital aleukocytosis.[2]

This paper presents a case of thymic alymphoplasia, associated with generalized lymphoid depletion, hypogammaglobulinemia, and pancreatic fibrosis with cystic changes and mucoviscidosis in a male who succumbed to overwhelming infection at the age of 10 weeks.

Patient K.R. was admitted to Milwaukee Children's Hospital on July 2, 1964, at the age of 6 weeks, because of vomiting and diarrhea. He was the product of an uneventful pregnancy of a gravida IX para-gravida VIII mother and had a birth weight of 8 lb. 6 oz. The neonatal period was uneventful except for some irregularity in bowel movements. These became regular at home and there were no problems until three days before admission. The boy was fed on Similac®, approximately 26 oz. daily. He started coughing three days before admission, followed by projectile vomiting after feedings on the next day. Diarrhea started at approximately the same time. On the day of admission there was bright red blood in stools. No treatment had been given.

On admission he was small and thin, weighing 8 lb. 4 oz., and had a severe diaper rash. His skin turgor was not remarkable and the mucous membranes were moist, but the eyes were slightly sunken and the conjunctivae injected. Heart and lungs were normal. The abdomen was soft and neither organ enlargement nor any mass was noted. Rectal examination was unremarkable.

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Hemoglobin was 14.5 gm. percent, and hematocrit was 50%, with 11,800 white cells per cubic millimeter; differential was 45% segmented neutrophils, 54% lymphocytes, many atypical, and 1% monocytes. Chemistry studies revealed sodium 130 mEq. per liter, K 7.0 mEq. per liter, CO_2 19.4 mEq. per liter, Cl 92 mEq. per liter, and pH 7.42. The urine was unremarkable. Pyloric and chest X-rays were reported as normal.

A diet of tea and Lytren® was immediately started, but he continued to have watery stools through the next day. Purulent drainage from both eyes was treated with optic sulfacetamide drops. Intravenous Ionosol® and a neomycin preparation were started, and 100 cc. of plasma given. The white count rose to 18,900 per cu. mm. on July 4, but differential count, hemoglobin, and hematocrit showed little change. Barium enema was negative. Although watery stools continued, cultures over several days were negative for pathogens. Six days after admission the patient had gained 5 oz. Cough developed. Fluorescent antibody studies were negative for pertussis.

By July 8 hemoglobin and hematocrit fell to 6 gm. percent and 17%, respectively. Penicillin was followed by 80 cc. of whole blood. Posttransfusion hemoglobin and hematocrit rose to 11 gm. percent and 33%. Electrophoresis of serum proteins on July 8, after plasma and blood transfusion, indicated levels as follows: total protein 3.8 gm. percent with albumin 2.1 gm. percent, alpha-1 globulin 0.3 gm. percent, alpha-2 globulin 0.5 gm. percent, beta globulin 0.6 gm. percent, and gamma globulin 0.3 gm. percent. Hemoglobin dropped to 5 gm. percent over the next two days and hematocrit fell, while the leukocyte count rose to 38,500 per cubic millimeter (80% segmented neutrophils). A rectal biopsy on July 14 had normal ganglion cells, but as the mucus-secreting glands were active and were slightly dilated, the report indicated that the tissues

TABLE 1

Date	Hemoglobin	Hematocrit	White blood count	Segmtd. cells	Lymphocytes	Bilirubin direct total	Sweat chloride	Stool trypsin	
7/3/64	14.5	50	11,800	45	54				Na 130;K 7.0; CO_2 19.4; Cl 92; pH 7.42 250 cc. pooled plasma
7/4	13.0	39	18,900	57	39				Na 13.5; K 5.7; pH 7.40
7/6			11,300	59	41		15.6		Cult. FTA pertussis-negative Eye-H. aegyptus
7/8	6.0	17	16,100	90	10	0.5/2.2	8.2		Coombs: negative. Reticulocytes 5.6%. G-PD-263 units. 15 cc. whole blood. 80 cc. whole blood
7/9	5.5	22							
7/10	11.0	33							FTA pertussis-negative
7/11	9.0	28	38,500	80	16			3+	Prothrombin 68%. 30 cc. salt-poor albumin. 160 cc. platelet-rich blood
7/13	6.5	22	29,200	68	16				Platelets 48,000 per cubic millimeter
7/14	12.0 11.5	36 39							Rectal biopsy—ganglion cells present; dilation of some glands consistent with mucoviscidosis
14.0	7/15	44				16.5/22.2			
7/16	11.5	36				30/35.4			SGO-T 29 SGP-T 12
7/17	11.5	35	54,600	82	15	1.8/2.8			
7/18	10.0	32	22,100	89	11	1.3/1.5			
7/19	8.4	28							
7/20	8.5	25							
7/21	7.0	23	12,200	80	19		17.0		Platelets 21,000 per cubic millimeter
7/22	8.0	24	8,000	75	25				5 cc. whole blood
7/23	6.0	20	8,100	68	28				
7/24	5.5	19							
7/25	5.0	17							125 cc. whole blood
7/26	9.0	30							
7/27	9.0	27				7.2/8.4		+	
7/28	8.5	24				14.0/17.0			Na 137; K 3.3; CO_2 18.9; Cl 112; pH 7.37. Plasma hemoglobin 24
7/29	8.0	25							LE negative × 2 Plasma hemoglobin 63 and 45

Negative X-rays; pyloric series, chest, barium enema, skull.

Protein electrophoresis: 7/10 Alb. 2.1; α1-0.3; α2-0.5; β-0.6; α0.3; Total 3.8 gm.
7/21 Alb. 1.8; α1-0.4; α2-0.5; β-0.5; α0.3; Total 3.5 gm.

were "consistent with mucoviscidosis." Stool was strongly positive for trypsin and negative for occult blood. Sweat chloride levels were 15.6 and 8.2 mEq. per liter.

On July 15 the boy was jaundiced; his liver edge was palpable just below the right costal margin. Total bilirubin was 22.2 mg. percent, of which 16.5 mg. percent was conjugated, and this rose to 30 mg. percent (35.4 mg. percent total) the next day. Stools were clay-colored and pasty. Alkaline phosphatase, serum glutamic oxalpyruvic transaminase (SGO-T) and serum glutamic pyruvic transaminase (SGP-T) were within normal limits. The next day the jaundice cleared, stools returned to brown color, and bilirubin dropped to normal levels, but the temperature spiked to 102°. White blood count rose to 54,000 per cubic millimeter (82% segmented neutrophils). A macular red rash was noted, mostly on the abdomen. On July 18 the liver was palpable 6 cm. below the right costal margin. White blood count was 22,100 per cubic millimeter (89% segmented neutrophils); hemoglobin was 7 gm. percent.

The child's condition continued to deteriorate; his hemoglobin dropped to 7 gm. percent and platelets to 21,000 per cubic millimeter by July 21. Serum electrophoresis results were essentially as before, with low levels throughout. His cough became worse and more paroxysmal. One hundred and twenty-five cubic centimeters of whole

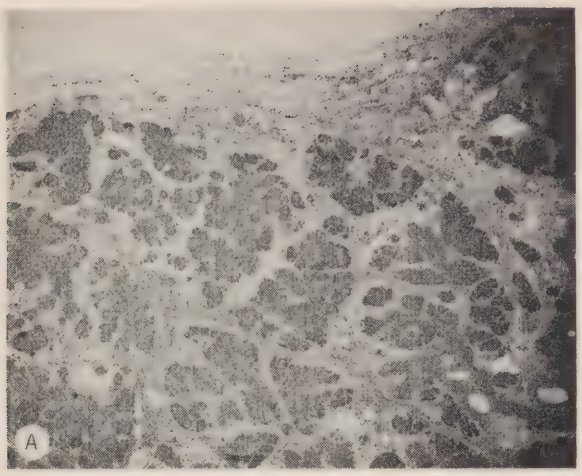


Fig. 1. A. Section from the thymus of patient K.R., showing the small lobules and separating broad connective tissue bands. The thick capsule can also be seen. 40 ×

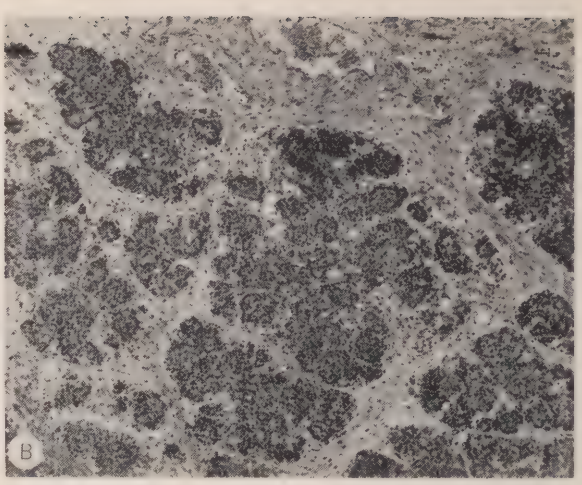


Fig. 1. B. Higher magnification of the same area. 95 ×. There is no differentiation into cortex and medulla and Hassall's corpuscles are not present.

blood were given on July 25, after the hemoglobin had reached 5.0 gm. percent. Sweat chlorides were 17.0 mEq. per liter. By July 27 the boy became edematous and lethargic; at this time he was again icteric. Bilirubin was 7.2 mg. percent conjugated and 8.4 mg. percent total. On the evening of this day he developed generalized seizures accompanied by irregular pulse and respiration. The seizures were controlled by paraldehyde. Steroids were started. The boy appeared to be resting quietly on the evening of July 28 and breathing was more regular, but early the next morning he was found dead in his crib.

POSTMORTEM FINDINGS

The body, showing fair development and nutrition, weighed 4,350 gm. Heart and great vessels, thyroid, central nervous system, peripheral nerves, and ganglia were not remarkable. There was general congestion and edema. Findings in thymus, lymph nodes, spleen, pancreas, lungs, liver, bone marrow, and adrenals follow.

The thymus (Fig. 1) weighed 1 gm. and measured 0.5 × 1.5 × 2.0 cm. It consisted of numerous small lobules separated by broad connective tissue septa and covered with a thick capsule. There was no differentiation into cortex and medulla; lymphocytes were virtually absent and Hassall's corpuscles were not seen. The cells in the lobules had slightly eosinophilic cytoplasm with indistinct borders and oval to slightly elongated reticular pale nuclei with fine, evenly distributed chromatin and rather prominent nucleoli.

The lymph node (Fig. 2), of normal size, showed no primary follicles or germinal centers and contained only very small numbers of lymphocytes. Most of the cells were of reticular type, similar to those seen in the thymus. Of the plasma cells present, only a few had the normal appearance; many had faintly eosinophilic cytoplasm and others did not show the usual spokewheel arrangement of the chromatin. The sinuses contained large numbers of phagocytes, many filled with hemosiderin.

The spleen (Fig. 3) was severely congested and contained very large numbers of hemosiderin-filled phagocytes. The corpuscles were atrophic and consisted almost entirely of cells with abundant eosinophilic cytoplasm and nuclei, resembling the reticular cells in lymph nodes and thymus.

In the gastrointestinal tract (Fig. 4), no primary follicles were seen and the lamina propria contained only occasional lymphocytes and plasma cells. The cell population consisted almost entirely of reticular cells.

The pancreas (Fig. 5) was of normal size, shape, and color, but firmer than usual. It consisted of lobules having increased fibrous tissue

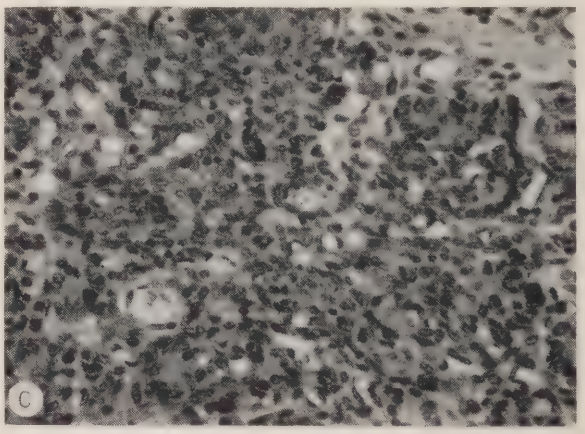


Fig. 1. C. Section from a lobule made up almost entirely of reticular cells. 370 ×



Fig. 2. A. Section of lymph node of patient K.R., showing absence of follicles. 40 ×

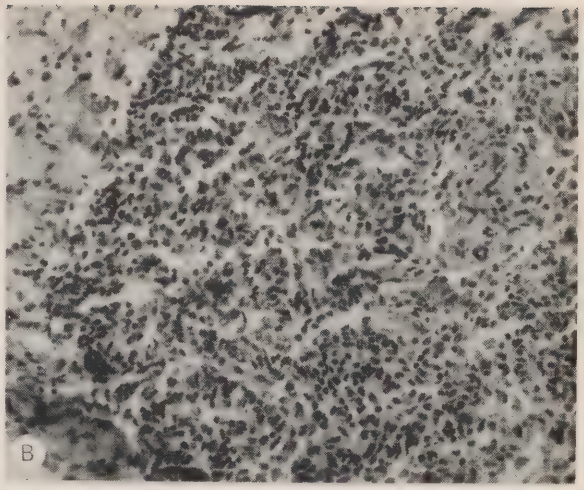


Fig. 2. B. Higher magnification (230 ×) to show rarity of lymphocytes.

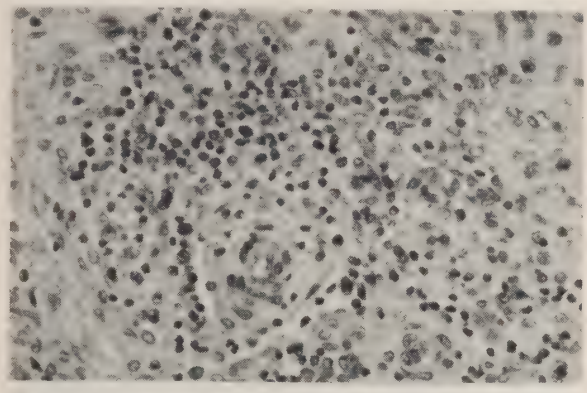


Fig. 3. Section of spleen of patient K.R., showing a Malpighian corpuscle; it consists of reticular cells and few lymphocytes. 370 ×

and atrophic and dilated acini containing eosinophilic material. The interlobular septa were thickened by fibrosis, while the ducts were dilated and contained eosinophilic material.

Severely congested lungs demonstrated large areas of hemorrhage, emphysema, and atelectasis. The sero-mucous glands of larynx, trachea, and major bronchi were dilated.

In the liver, there was severe congestion; most Kupffer cells contained hemosiderin granules. There were many small areas of coagulation necrosis with no inflammatory reaction. Special stains failed to reveal fungi, bacteria, or other microorganisms. The bone marrow consisted almost entirely of osteoblasts and osteoclasts. Adrenal glands showed cortical lipid depletion.

FAMILY HISTORY

The mother and father are apparently well. The mother is a gravida IX, para-gravida VIII. Five children are alive and well.

R.R. was born on March 17, 1956, with imperforate anus and malrotation of the bowel and died at the age of 11 months from what was thought to be bronchopneumonia. Autopsy permit was not granted, but repeated chest X-rays were suggestive of pulmonary fibrosis and the radiologist raised the possibility of cystic fibrosis of the pancreas.

D.R., born on May 11, 1963, died at 2 months from gastroenterocolitis and septicemia. Pseudomonas aeruginosa was recovered from heart blood and bowel contents. There was ganglionic agenesis of the colon in the distal 3 cm. segment and, in addition, fibrosis and cystic change of the pancreas associated with dilation of mucus-secreting glands, including Brunner's glands and those of colon, larynx, and trachea. A purpuric rash involved head, neck, upper portions of extremities, and trunk. The thymic changes were initially thought to be associated with the septicemia. Review showed the thymus (Fig. 6), as in the present case, to consist of immature lobules separated by broad connective tissue bands. The lobules, with no differentiation into cortex and medulla, few lymphocytes, and no Hassall's corpuscles, consisted of cells morphologically identical to those in the subject of this report. In sections from large and small intestine (Fig. 7), follicles and germinal centers were absent and lymphocytes were few. There was reticular hyperplasia. Plasma cells were absent in gut and spleen. The pancreas (Fig. 8) was similar to that of the brother reported here. This case was not included in the presentation because there were no absolute lymphocyte counts or serum protein studies. Anatomical findings, the clinical course, and the overwhelming infection causing death are, however, in close agreement with those of his brother.

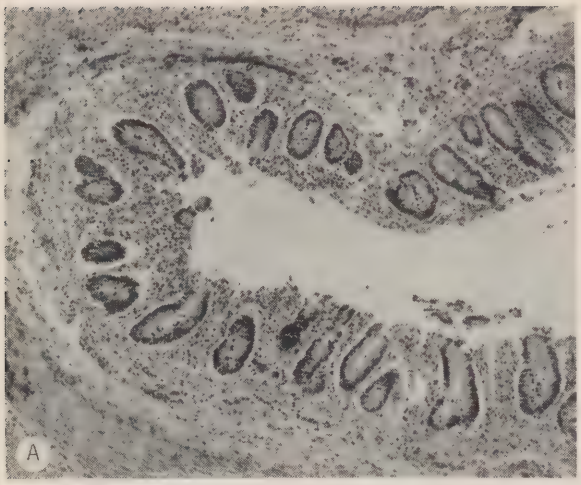


Fig. 4. A. Section from colon of patient K.R. shows absence of follicles. 95 ×

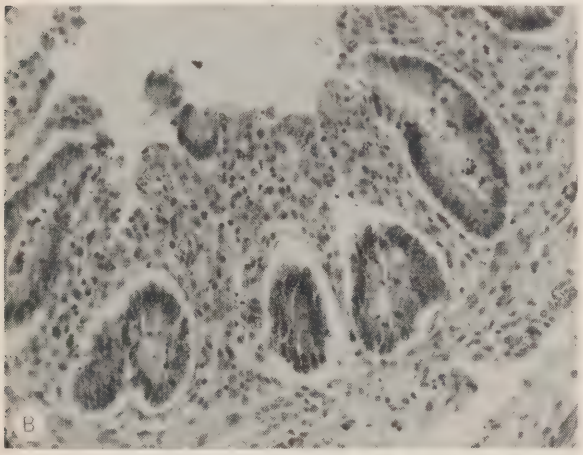


Fig. 4. B. Higher magnification (230 ×) of same area, revealing reticular hyperplasia and virtual absence of lymphocytes in the lamina propria.

COMMENTS

In the patient's course, several things need explanation. First, it is believed that infection was present; one blood culture produced Str. faecalis, although a later one was negative. In the hospital there was progressive increase in the leukocyte count, up to 54,600 per cubic millimeter and of the segmented neutrophils, up to 82%. In the last week the leukocyte count dropped to 8,000 per cubic millimeter, but of these there was 75% segmented neutrophils. The autopsy cultures from heart, blood, lung, and middle ear all produced Pseudomonas aeruginosa despite the repeated antibiotic treatment. The blood cultures, in addition, produced escherichia.

The anemia may be explained on the basis of bone marrow depression by the toxic products of infection, hemolysis (there was severe hemosiderosis of spleen and liver), and hemorrhage. The changes in serum bilirubin levels lead to speculation. In one occasion the level was 35.4 mg. percent total (30 mg. percent direct), and the next day it dropped to 1.5 mg. percent total with 1.3 mg. percent direct. Concomitantly, the stool color changed from clay to brown. The above suggest relief of temporary plugging of bile passages, extra or intrahepatic. At autopsy there was no evidence of obstruction, but the gallbladder contained mucoid material and the cystic duct was filled with thick viscid bile. The slight increase in unconjugated bilirubin is accounted for by hemolysis and hemorrhage.

DISCUSSION

In mice,[3–6] rats,[7–9] and hamsters,[10,11] thymectomy at birth or shortly thereafter results in a fatal wasting disease, marked diminution in the population of small lymphocytes in the blood

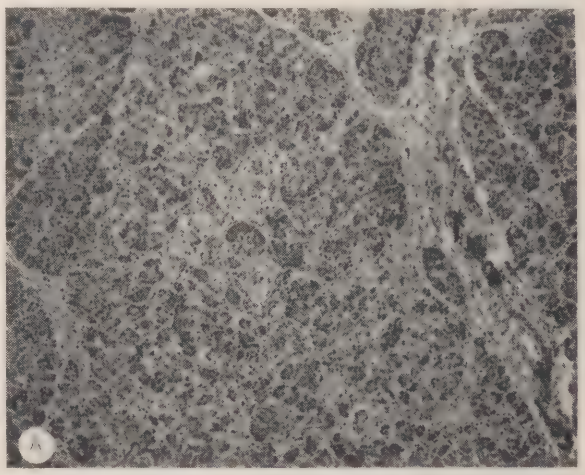


Fig. 5. A. Section from the pancreas of patient K.R., showing interlobular and intralobular fibrosis and several dilated ducts and acini. 95 ×

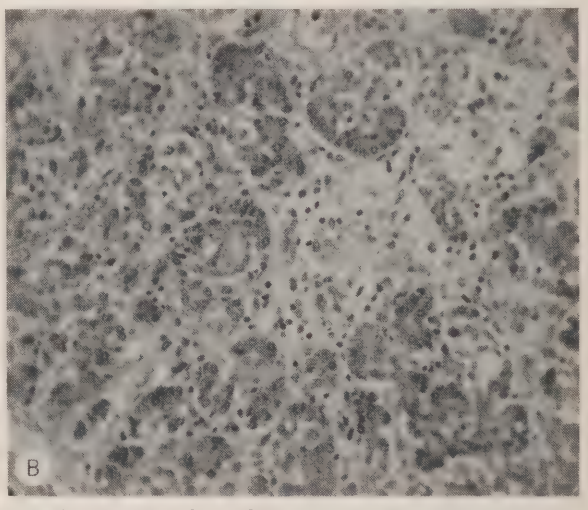


Fig. 5. B. Section from the same area showing the fibrosis and the dilated acini, some containing plugs. 230 ×

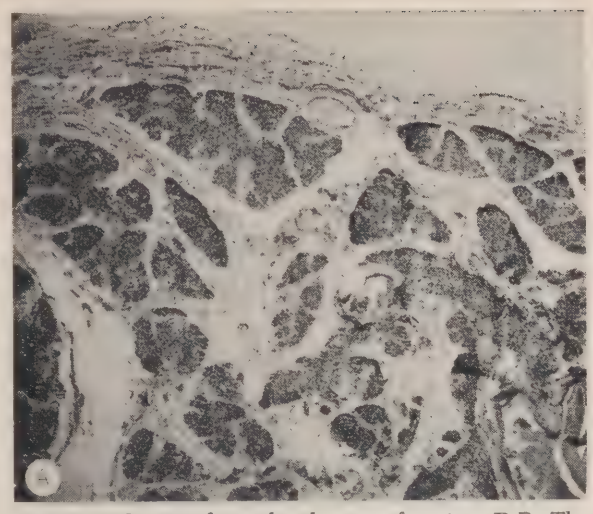


Fig. 6. A. Section from the thymus of patient D.R. The similarity to the thymus of patient K.R. is evident. 40 ×

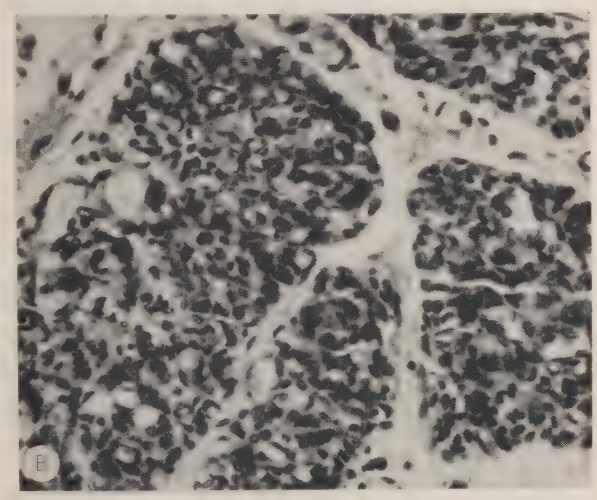


Fig. 6. B. At higher magnification (370 ×), the absence of cortico-medullary differentiation and Hassall's corpuscles, and the rarity of lymphocytes can be seen.

and tissues, diminished capacity to produce serum antibodies, and failure to reject foreign tissue grafts.

The thymus, then, is important for the development of the immune apparatus, although the mechanism has not been clarified. A humoral and a cellular hypothesis are discussed by Miller,[12] and there has been support for both.[13–17]

How may this apply to man? Glanzmann and Riniker[18] reported 2 cases of lymphopenia in siblings who died from oidium albicans infections at 5 and 6 months. At autopsy, loss of lymphocytes in gut, lymph nodes, and spleen with proliferation of reticular cells was found. The thymus in the one case was described as pale, edematous, and weighing 15 gm., and in the other as small, edematous, and very pale.

Hitzig and Willi[19] presented 4 cases characterized by familial incidence, malignant, therapy-resistant infection, pronounced lymphopenia, and agammaglobulinemia. At autopsy, they found almost complete absence of the lymphatic system with much replacement by reticular cells.

Gitlin and associates[20] in 4 children with "congenital agammaglobulinemia" and severe recurrent infections found, at autopsy, lymphoid depletion with no germinal centers or plasmocytes in the lymph nodes, gut, and spleen. In 2, the thymus had no lymphocytes or Hassall's corpuscles.

Gitlin and Craig[1] reported 15 patients with "congenital agammaglobulinemia," of which 6 were associated with lymphopenia. All these 6 children had succumbed to infection by 24 months. At autopsy, there was lymphoid depletion with absence of germinal centers in lymph nodes, spleen, and gut. Plasma cells were either



Fig. 7. A. The section shows absence of lymphoid follicles from the colon of patient D.R. 40 ×

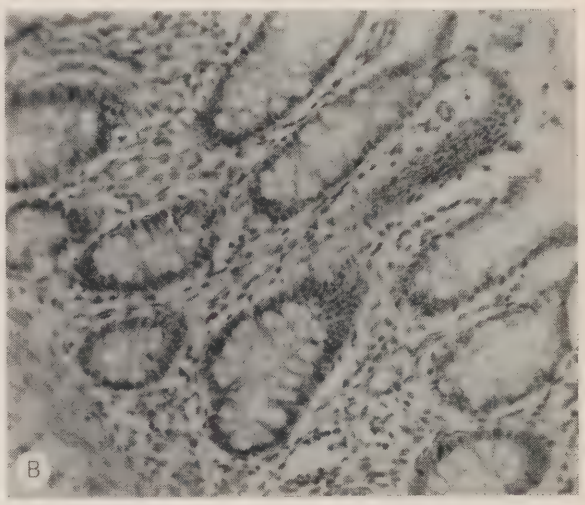


Fig. 7. B. Higher magnification (230 ×) shows few lymphocytes and no plasma cells in the lamina propria.

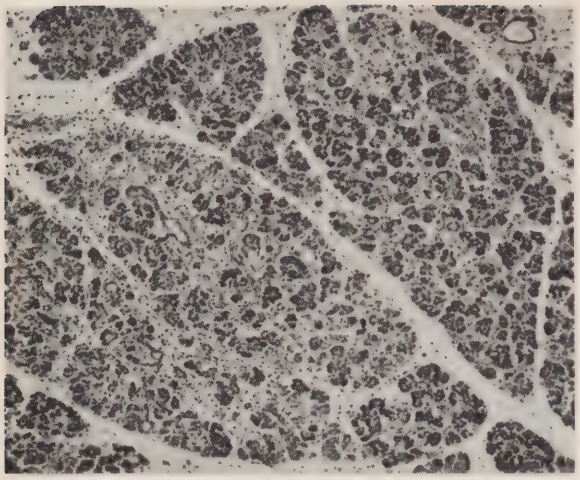


Fig. 8. Section from the pancreas of patient D.R., showing interlobular and intralobular fibrosis and dilatation of ducts and acini. 95 ×

absent or atypical. The thymus, available in 5, consisted of poorly developed lobules separated by broad strands of connective tissue; there was no differentiation into cortex and medulla and no lymphocytes or Hassall's corpuscles. The cells resembled reticular cells.

Last, in a little girl who died from an overwhelming infection at the age of 15 days and who had aleukocytosis, Gitlin and associates[2] described postmortem findings similar to those in the cases of congenital agammaglobulinemia with lymphopenia.

The above cases have familial incidence, severe recurrent fatal infections, and generalized lymphatic hypoplasia. Because of the occurrence of all the other features, it would be tempting to assume that in Glanzmann's and Hitzig's cases the thymus was immature as in the cases of Gitlin. Here, then, we are presented with something very similar to what happens to the laboratory animal thymectomized at birth, except that in the human being there seems to be an inherited arrest in the development of the thymus.

We think that our case and his sibling, D.R., belong to the above group. In K.R. we had no absolute lymphocyte counts, but the microscopic appearance of the thymus; the tremendous reduction in the number of small lymphocytes in the gut, lymph nodes, and spleen; the hypogammaglobulinemia; and the clinical symptomatology with infection causing death despite treatment are enough to classify it in the thymic alymphoplasia group. Fibrosis and cystic changes of the pancreas and mucoviscidosis in intestine and respiratory tract were also present in both cases.

SUMMARY

The evidence[1] suggests that thymic alymphoplasia is an inherited developmental anomaly of the thymus resulting in generalized lymphoid hypoplasia with crippling of the immunological reactivity of the body. The findings in our patient and his sibling support and strengthen the evidence already present. In addition, our 2 patients had fibrosis and cystic changes of the pancreas and generalized mucoviscidosis which, for the first time, are reported in association with thymic alymphoplasia.

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Copper Sulfate as an Emetic

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As THE ingestion of toxic materials constitutes one of the commonest emergency room problems, there are good reasons to have well-established procedures to meet the problem.

When the material ingested is not corrosive the first step in treatment is to empty the stomach. This can be accomplished by using a large-bore soft rubber tube to empty and lavage the stomach. The second method available is to induce emesis by mechanical gagging, using orally effective emetics, or by the injection of apomorphine.

There are numerous references to the effect that emesis is a superior method of effectively emptying the stomach. The presence of large food particles or relatively insoluble toxic agents frequently precludes the efficient cleansing of the stomach by lavage.

The two principal ways in which orally administered emetics act are by direct gastric irritation and by reflex stimulation of the hypothalamus. Mustard is the most frequently used material for direct gastric irritation and is a fairly effective emetic agent. Syrup of ipecac and copper sulfate are the commonly employed agents acting by the stimulation of the hypothalamus.[1]

While syrup of ipecac has been established as an effective agent it has been associated with accidents when the more potent fluid extract of ipecac has been substituted for one reason or another. It also deteriorates after a period and therefore needs to be renewed.

Copper sulfate is a local irritant as well as an effective stimulator of the hypothalamus. For emergency room use, single doses of the dry powdered crystals may be prepared in individual containers. These may be stored indefinitely without deterioration.

For many years the late Dr. R. O. Bassuener employed copper sulfate as an emetic at Johnson Municipal Hospital. Based on his experience we have used it as an emetic in several Milwaukee treatment centers during the past three years.

In order to review the effectiveness of the use of copper sulfate as an emetic, we have observed its use in 100 pediatric patients.

Aspirin ingestion, as is generally true, provided the greatest number of cases, with lesser numbers of other drugs and household product ingestions. These are categorized as follows:

TABLE 1

Material ingested	*Number of patients*
Aspirin and other antipyretics	53
Laxatives	7
Mothballs	6
Alcohols, rubbing and wood	4
Antihistamines	3
Mushrooms	3
Bathroom materials and cleansers	3
Sulfonamides, barbiturates, amphetamines, and ataraxic drugs	8
Atropine, cigarettes, glue, and calamine and diphenhydramine hydrochloride (Caladryl®)	4
Unknown	9
	100

In several instances more than one toxic material was ingested.

Each patient was given 250 mg. of copper sulfate prepared by placing the dry salt in a 1-oz. bottle. The bottle was filled with tap water and the patient drank the medication directly from it. The time elapsing to vomiting, the effectiveness of the vomiting, and the decision to use additional treatment were observed in each instance.

Vomiting generally occurred soon after the copper sulfate was administered. Table 2 shows the time elapsing before vomiting and whether or not supplementary treatment was required.

In an attempt to evaluate the other factors of effectiveness, the emesis produced was classified as to apparent effectiveness. The results are shown in table 3.

In 75%, the emesis was rated as highly effective,

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TABLE 2

Number of patients	*Minutes elapsing*	*Cumulative*
3	Immediate	
27	3 minutes†	30
33	5 minutes	63
19	10 minutes	82
8	15 minutes	90
1	20 minutes	91
1	25 minutes*	92
1	40 minutes†	93
7	Over‡	100

*10 ml. syrup of ipecac were given ten minutes after copper sulfate.
†Vomited immediately after a second dose of copper sulfate.
‡Never vomited, were lavaged after ten to forty minutes.

TABLE 3
EFFECTIVENESS OF THE VOMITING

Vomiting, degree of effect		*Supplementary measures* *Lavage*	*2nd emetic*
Massive, projectile	75	1	
Moderate, effective	12	1	
Ineffective, small	3	3	1
No vomiting	10	8	3
	100	13	4

and an additional 11% was rated satisfactorily effective, giving a total of 86% effective. Only 4 of the patients with an unsatisfactory result were given a second emetic. Two were given syrup ipecac and vomited adequately after additional lapses of ten and fifteen minutes. One was given a second dose of copper sulfate and vomited effectively, immediately. Another was given a second dose of copper sulfate without effect and was lavaged after waiting a total of thirty-five minutes.

In 8 patients, lavage was employed after waiting ten to thirty minutes for vomiting. No doubt some of these would have responded to a second dose of copper sulfate.

From these observations we can conclude that effective vomiting follows the administration of 250 mg. of copper sulfate dissolved in 1 oz. of water in 86% of the patients and that vomiting occurs within fifteen minutes in 90% of the patients. Though not tabulated, all of the effective emesis occurred within fifteen minutes.

A routine can be outlined from these observations. Emesis for the ingestion of toxic or potentially toxic but noncorrosive materials may be induced by the administration of 250 mg. of copper sulfate. If vomiting does not occur to a satisfactory degree within ten minutes, a second dose may be given. If this is not followed by effective vomiting within five minutes, the patient should be immediately treated by lavage.

SUMMARY

The results of employing 250 mg. of copper sulfate to induce emesis in 100 cases of ingestion of noncorrosive toxic materials have shown that effective emesis ensues in 86% of the patients within fifteen minutes.

Emptying the stomach in cases of ingestion of noncorrosive toxic materials may be accomplished by the administration of 250 mg. of copper sulfate dissolved in 1 oz. of water. If ineffective within ten minutes, a second similar dose should be administered. If the second dose is ineffective for five minutes, the stomach should be emptied by lavage.

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CHOLESTEROL VALUES are useful in predicting relative risk of coronary artery disease. The risk rises as values increase within the normal range and beyond, but no critical value exists below which coronary attack does not occur nor above which an attack is inevitable. An average value obtained by repeated determinations is necessary to classify individual risk accurately. Highest risk is for persons with high cholesterol values plus elevated blood pressure. For persons with high blood pressure and low cholesterol the risk is comparable to that for persons with high cholesterol and low pressure. Men with values of 260 mg. percent or more have coronary attacks more than 4 times as often as those with values lower than 200. An equation expresses a more meaningful concept of risk of myocardial infarction than setting normal values. Risk $= a + b(\text{chol.})^3$, where risk is equal to a constant that represents the portion of coronary risk unrelated to cholesterol plus a constant representing cholesterol contribution multiplied by the cholesterol value raised to the third power.

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Pulmonary Amoebiasis of Right Upper Lobe

K. S. GREWAL, M.D., and R. P. DIXIT, M.D.

Rourkela, India

NONBASAL PULMONARY AMOEBIASIS is rarely diagnosed even in countries where intestinal amoebiasis is an endemic and frequent disorder.

Cases of nonbasal pulmonary amoebiasis have been reported by several authors.[1,3,6,7] Bunting,[3] in 1906, was first to describe a hematogenous lung abscess. Manson-Bahr,[4] in 1923, described 3 cases without liver involvement and named it primary pulmonary amoebiasis.

We present the following case.

CASE REPORT

Shri Manbodh, male, aged 40, was examined and found to have a productive cough containing 4 to 6 oz. of mucopurulent discharge, with an intermittently high fever accompanied by rigor during the past week. He gave a six-month history of dysentery. Other important antecedent chest or systemic disease was not reported. No history of contact with tuberculosis was given. He had been a moderate smoker. On examination the patient was a well built man with pronounced pallor and toxemia. His temperature ranged between 101° F. to 103° F. Chest examination revealed slightly impaired breath sounds and coarse crepitations below the clavicle, pectoral, and upper axillary area on the right side. The liver was not palpable. Examination of other systems was noncontributory. A chest X-ray dated June 11, 1963, showed a homogenous opacity in the right upper lobe. Hemogram showed a leucocyte count of 13,200 per cu. mm., with 80% polymorphs, 12% lymphocytes, 2% monocytes, 6% eosinophils and a hemoglobin of 10 gm. percent. Repeated examinations of sputa were negative for acid-fast bacteria. A sputum culture showed normal flora. The urinalysis was negative. The stool showed hookworm ova. Bronchogram on June 7, 1963, showed a normal bronchial tree. He was treated with a combination of streptomycin sulphate and penicillin (Streptopenicillin®) and oxytetracycline (Terramycin®) and discharged on July 14, 1963, as a case of unresolved pneumonia. He was advised to have regular checkups at the outpatient clinic because his symptoms and radiological lesion persisted. The patient was readmitted on Aug. 14, 1963, with a high fever, rigor, chills, pallor, toxemia, and a productive cough which was occasionally bloodstained. An X-ray dated Aug. 14, 1963, showed a persistent, former right lung lesion. Hemogram showed a total of 13,800 leukocytes per cu. mm., with 78% polymorphs, 16% lymphocytes, and 6% eosinophils. Urinalysis was negative. Repeated sputum examinations were again negative for acid-fast bacteria, and a culture showed normal flora. Stool examination was negative for Entamoeba histolytica. In view of the failure to respond with antibiotics and failure to isolate acid-fast bacteria or other pathogenic organisms in sputa, it was thought worthwhile to give a course of emetine. Sputum examination for amoeba was negative. The bronchorrhea markedly diminished after 3 gr. of emetine and the patient was asymptomatic in a week. X-ray taken after 10 gr. of emetine showed radiological clearance of the lung lesion. The patient was discharged on Aug. 29, 1963.

DISCUSSION

Diagnosis of amoebic lung lesion without direct proximity to the liver is difficult even where amoebiasis is prevalent. The disease is not rare—although reports in literature are few. Abdel Shaffi,[2] in 1952, reported the incidence of lung abscess in various locations in 1.6% necropsies. High prevalence in this and other necropsy material strongly indicates that the nonbasal amoebiasis is a commoner condition than believed hitherto. Various routes of infection have been suggested. Systemic embolism to the lung through the middle and inferior hemorrhoidal veins draining the anorectal area is the most accepted route. Hematogenous emboli can originate in the thrombosed hepatic veins and can reach the inferior vena cava and lodge in the pulmonary capillary bed. Lymphatic spread across the diaphragm is considered to be the usual

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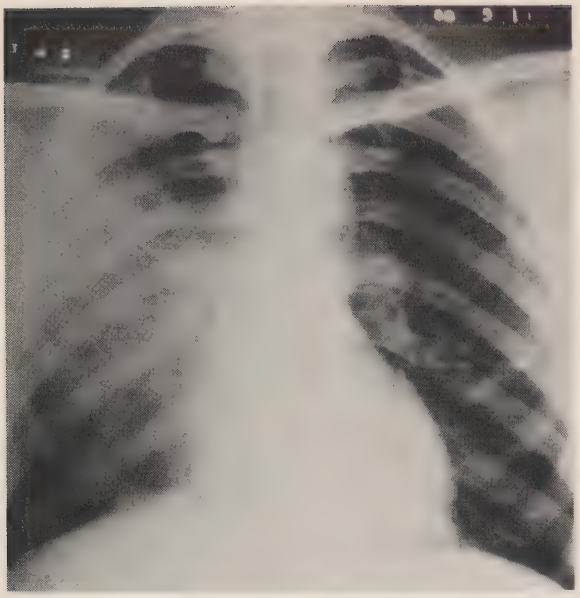


Fig. 1. Pulmonary amoebiasis of right upper lobe. First X-ray, June 11, 1963



Fig. 2. Pulmonary amoebiasis of right upper lobe. Second X-ray, Aug. 14, 1963

route of the basal amoebic lung lesion. Existence of specific amoebic bronchitis is doubtful.

As stated above, clinical diagnosis of nonbasal pulmonary amoebiasis is difficult. Symptoms of intermittent fever, pallor, pronounced anorexia and cough with purulent or mucopurulent sputum which is occasionally blood stained are usually present. A history of dysentery may or may not be elicited. The bitter taste and chocolate-or anchovy-sauce-colored sputum are due to liver pus and characteristic of basal amoebic infection.



Fig. 3. Pulmonary amoebiasis of right upper lobe. Third X-ray, Aug. 25, 1963

In nonbasal amoebiasis this characteristic is conspicuous by its absence. The liver may be enlarged or tender if there is associated hepatitis. Stool examination for Entamoeba histolytica and sigmoidoscopy may give contributory evidence. A thorough search for amoeba in sputum should be done, but is rarely successful.[5] Amoebas have been found in sputa by Warrakir[6] and others.

The diagnosis of nonbasal pulmonary amoebiasis should be kept in mind when a history of dysentery or enlarged and tender liver is associated with intermittent high fever, pallor, anorexia, moderate leukocytosis with granulocytosis, and eosinophilia. Failure to respond with antibiotics and persistence of radiological opacity, which is unaccountable by microbial flora of sputum, are highly suggestive. Indirect proof of the etiology is obtained by therapeutic trial of emetine. The response is dramatic and lasting.

We are grateful to Dr. B. S. Dhillon, M.B., F.R.C.S. (Eng. & Edin.), Chief Medical Officer, Ispat General Hospital, for his constant encouragement, valuable advice, and kind permission to publish this case.

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William F. Sihler, M.D.

KATHLEE SIHLER PALMER
Cando, North Dakota

"It was 30 below zero on that 5th day of January 1899, when I arrived in Grand Harbor, North Dakota. I had on a little light overcoat with a velvet collar, you know the kind; a stiff hat, one of the ancient 'bowlers'; and a beautiful pair of fine kid gloves. I also carried a cane, which I hooked over my arm as I got ready to step off the train. Wilson, the man who met me, stood on the platform, covered with a big fur coat, his cap coming down so that all I could see was his eyes. . . . He had felt shoes on, and he looked pretty much like a big brown bear."

In this manner, Dr. Sihler described his introduction to North Dakota.

William Frederick Sihler was born in Simcoe, Ontario, Canada, June 13, 1876, the ninth of ten children. His preliminary education was at Simcoe high school and Trinity College, Toronto, from which he graduated cum laude in 1894. He entered the medical school of McGill University at Montreal the following autumn. He interned at General Hospital, Montreal, for general practice, and later returned to McGill for postgraduate work in surgery.

"It was in July, 1898," Dr. Sihler said, "that I arrived home from the university with all the requisites to practice medicine, including a real sheepskin decorated with ribbons and the names of many famous medical men. My oldest brother was a graduate from the same school fifteen years before, and had been the instigator and financial factor that had made it possible for me to go to college. Brother was then practicing in Litchfield, Illinois, and had 3 sons contemplating and already preparing to be doctors and to graduate from McGill."

In search of a location to practice, young Dr. Sihler took the family horse and buggy to drive 25 miles from Simcoe to Brantford, Ontario, to talk with a Dr. Lamont who had practiced in partnership with Dr. Harris of Cando, North Dakota. Dr. Lamont was very enthusiastic about the Midwest and its great opportunities and encouraged Dr. Sihler to go out and look over that region in North Dakota.

The first impression of the snow wrapped prairie was a bleak one indeed, but since young William had only $30 in his pocket, and since the need for a doctor in that community was so acute, he decided to stay for the remainder of the winter.

The territory he was to serve was vast, and his only means of transportation then was by livery rig, "composed of a sleigh and a couple of broncos, not very fast or substantial," or else by going with relatives or a friend of the patient.

This profile was prepared at the request of JOHN C. FAWCETT, M.D., *Devils Lake, North Dakota.*

The roads at that time were a problem. In fact there were no roads at all and it was a matter of going around snowbanks and across ditches. In the summer there were only prairie trails.

Another problem was keeping warm on the trips. "I had a very large coonskin coat which I had brought with me from Montreal. It had a large square collar that would come right up to the top of my head, and a fur wedge cap that I could pull down so that all that was exposed was my eyes. I had some ladies take a cowhide and make a sack out of it, leaving the fur on the outside, and lining it with a blanket with the bottom of sheepskin. The sack was so large that I could step right into it, poke my fur coat right down inside, and pull the sack up around my armpits. I could ride for hour after hour this way and not get too cold. If I did upset, I would just roll out of the sack, and after getting the sleigh straightened out, I would get back into the sack and after a mile or two, I would be fairly comfortable again."

After almost two years, Dr. Sihler moved to Devils Lake, 7 miles east of Grand Harbor. The next year he returned to Canada for Christmas. Before returning to Devils Lake he married Anna Alberta Matthewman of Ottawa, a girl he had known his senior year in college. In June the following summer, Mrs. Sihler joined the doctor in Devils Lake where they lived at the Sevilla, which is now the Grayson Hotel, until they bought a home on Seventh Street.

In 1905 Dr. Sihler bought his first car, a Stanley Steamer which he could use only during the summers. "We always had a lot of trouble with the farmers' horses. They didn't like the automobile and behaved as though they never were going to like it . . . but it was certainly an advantage to be able to get into the car and make long distance calls, even if we could go only twenty or twenty-five miles an hour." Forty years later, Dr. Sihler bought an airplane!

The manner in which Dr. Sihler progressed from the horse and buggy to the airplane typified his approach to progress in medicine. His first shock had been to the high mortality of mothers and babies, the lack of aseptic care, and the unnecessary and harmful internal examinations of some of the midwives and of being called in two or three days after a delivery to find the mother with a high fever and chills, and sometimes delirious with a case of puerperal septicemia. Dr. Sihler's first reaction was swift and sweeping. Out went the little old ladies with their little black bags. In his memoirs he says, "Called on to treat a woman, I found part of the afterbirth still protruding. I sent for the midwife and showed her what was going on. She threw her head back and her chest out, and said, "Well, I didn't put it there!"

"No," I said, "but you left it there when you shouldn't have! Now listen, any more of this kind of work going on here and I'm going to ask somebody to request a certificate of you that you are entitled to practice medicine, and if you can't show a certificate, you will have to take the consequences."

From that time, Dr. Sihler began to dream of a hospital where not only mothers and babies would be cared for, but where nursing care and facilities would be adequate for successful surgery. Many of his first surgical cases were performed in the farm home, on the kitchen table, when necessity called for hasty improvision and great courage.

In 1905 Dr. Sihler went back to Montreal for postgraduate work and had quite an extended visit in the hospitals there; visits made more enjoyable because some of his former classmates were connected with them—some were heads of departments—and he had every facility at his disposal. In 1907 he set about establishing his own hospital in Devils Lake. Miss Brae, a graduate nurse from a Philadelphia hospital, had worked for doctors for several years. She took charge as superintendent and immediately made arrangements to enroll students in a training school.

The little hospital opened in June 1908, and soon had 5 probationers, 3 of whom were accepted as students for a three-year course. Dr. Sihler went down to St. Barnabas Hospital in Minneapolis and found a Miss Colson to take over the post of superintendent to release Miss Brae for full time duty in the operating room and in surgical care.

At last Dr. Sihler had a hospital where histories of the patients were taken, where progress charts were kept, where there was a nurse and student on duty all night, every night, and where nursing responsibilities were assigned and accepted.

Governor John Burke appointed Dr. Sihler to the Medical Corps of the State Militia in 1909 and the first encampment was the following summer at Sparta, Wisconsin. Dr. Patterson of Lisbon was the Major, and Dr. A. W. McDonald and Dr. Sihler were Captains.

In 1911 the detail went to the San Antonio Third Field Hospital. While he was giving his credentials to Major Hartsock, Major Bob Patterson of the regular army and a former classmate of Dr. Sihler came along, and they had a very

happy reunion. Major Patterson later became U.S. Surgeon General.

By the fall of 1912 work was started on the basement of the new General Hospital and nurses' home. In March 1914 it was opened and Dr. Sihler practiced there for forty years.

Before the training school in the old General was started, there was not a graduate nurse in the country around Devils Lake. Doctors in the little towns around were calling constantly for nurses. They were willing to take even second-year girls but the superintendent vetoed that. Of those times, Dr. Sihler wrote, "We were doing a lot of work in those days and keeping the hospital pretty well filled with patients. Looking back, the ease with which we did it seems remarkable. There was plenty of help, and they were really interested in the hospital and in trying to get along with each other. They didn't mind if they were working an hour or two overtime, and seemed happy and contented. We did turn out some pretty good nurses, if I do say it. Over two hundred graduated during the years, according to the superintendent's count. One nurse out of our first class went to Rochester, and was an anesthetist for Dr. Bill Mayo. Others, after they returned from the war, got positions in large government hospitals. One was a supervisor in the Colonial Hospital in Rochester and while I was speaking with her one day, Charlie Mayo came along and took it upon himself to compliment me upon her ability."

During the years, Dr. Sihler made many trips to Rochester and was often urged by the brothers Mayo to join their staff, but he always felt he was doing a greater service by staying in Devils Lake, where he did considerable consultation work along with his own practice.

Doctors from as far north as Sarles, on the Canadian border, from Rugby, Brinsmade, Cando, Bisbee, New Rockford, Edmore, Lawton, Lakota, and McVille brought in patients. There were also a number of doctors on the Farmer's Line, one in almost every little town up to Hansboro. Dr. Sihler wrote, "All the fellows here in the district were fine chaps. They were well posted in their work. We seemed to get together more frequently socially, and would meet somewhere every once in awhile. We would always insist that a number of us would be at one of the medical meetings in the state."

In the early 1900's Dr. Sihler got the doctors together and the first district medical association was organized. Dr. Ruger was the first president, Dr. Thor Moller, secretary, and Dr. Sihler, vice-president. Dr. Fawcett of Starkweather, Dr. Emmert of Sarles, Dr. Beek of Lakota, and doctors from other towns came down for the meetings. They joined the state association and were one of the largest component associations of the state organization. This district association has been in existence ever since and at this time is very active.

In 1924 Dr. Sihler was appointed by Governor Nestos to the State Board of Medical Examiners, and continued to serve on the board under 5 governors until 1946. He has been a member of the North Dakota State Medical Association, serving as president in 1928. In 1920 he was made a member of the American College of Surgeons and a member of the International College of Surgeons in 1953. He has served as company surgeon of the Great Northern and Soo railways for over fifty years.

In 1928 Dr. and Mrs. Sihler spent the summer in Europe where they visited with their daughter who had been studying music in London and Paris for three years. Dr. Sihler also attended the Interstate Graduate Clinic Assembly. The meetings were in London, Prague, Munich, Berlin, and Vienna. Before and after the assembly, they toured most of the continent.

In his memoirs Dr. Sihler said, "I was especially interested in what the doctors were doing in other parts of the world; their attitudes toward the patients were completely clinical . . . the patients had no kind of relationship with the doctor that we find in America; and when I returned, I felt very well pleased about the work we were doing in this country."

For recreation Dr. Sihler liked to fish and hunt. The following hunting story is well worth recounting and almost unbelievable. "The geese came out of the lake against the wind, right over us. We shot until our ammunition was gone, and believe it or not, we had over ninety geese . . . we put these geese in a little square house in the center of the square at Grand Harbor, and intended that they should be used by anyone wanting a goose during the wintertime. The next fall we were out in the fields in the afternoon looking for chickens. Our dogs were perfect but they couldn't seem to find any. Later, discouraged, we started for home; then we noticed mallards coming down behind us and circling around a patch of barley that was still in the shock; there were hundreds-thousands of them! We tied the team and each one of us got into a shock of barley. It was just as bright as the moon could make it; it was beautiful. When the ducks came between us and the moon, we shot. After the flight, we picked up over two hundred ducks. We certainly figured that we would have enough meat for the village for all winter."

In later years, doctor didn't have the leisure for too much hunting and fishing but he loved the game of golf. There is a plaque in the beautiful country club that reads:

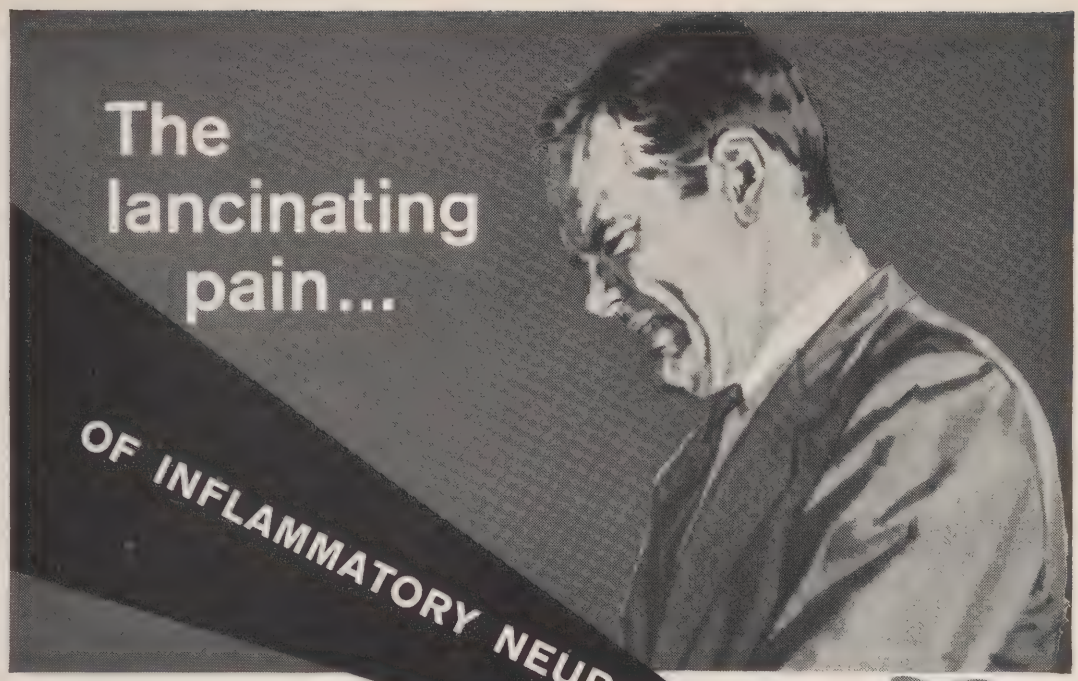
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Dr. Sihler is a member of the Episcopal Church, a Mason, Shriner and Jester. He belonged to the Rotary Club, joined the Woodman Lodge in Grand Harbor in 1889, and is a member of the Elk's Lodge and the Odd Fellows. In everything he did and belonged to, he stood for progress. He drove himself, as well as those associated with him, forward at a steady pace. Now retired, he should look back with considerable pride in his many accomplishments and contributions throughout the past sixty years. He has given of himself extravagantly, and he has done so eagerly. He not only dreamed fine dreams, but he built them into realities, for his own satisfaction, for progress, and for the good of his fellowman.

Dr. Sihler died Oct. 17, 1964. The above material was taken from his unpublished autobiography.

SYMPATHETIC DENERVATION of the upper extremity is best accomplished by second thoracic ganglionectomy. Denervation is the choice in severe disabling hyperhidrosis and the most useful surgical procedure in relatively serious occlusive or arteriospastic disease involving smaller arteries of the extremity. Postoperative recovery usually is smooth. General endotracheal anesthesia is employed with the patient either upright or facedown with the table head elevated and neck flexed forward. Incision is made at a right angle to the spinous process of the second thoracic vertebra. A muscle-splitting procedure is used to expose the vertebral end of the second rib and the transverse process of the second thoracic vertebra. About 2 to 3 cm. of the rib and outer half of the transverse process are resected subperiosteally. The mediastinum is entered between the first and second thoracic nerves. Pleura is dissected from the vertebral bodies. The ganglion beneath the second thoracic nerve is identified. The sympathetic trunk is grasped with a hemostat, and a silver clip is applied to the trunk below the stellate ganglion. Scissors are used to divide the trunk distal to the clip and proximal to the hemostat. The communicating rami are clipped and divided, the trunk is clipped below the second ganglion and divided with scissors proximal to the clip, and the ganglion is removed. Fresh frozen microscopic verification of ganglion is necessary since lymph nodes can be mistakenly removed. The wound is closed in layers without drainage. A postoperative roentgenogram is made to show which bone has been removed, the location of the clips, and possible partial pneumothorax. A sweating test is done six to seven days after operation.

J. GRAFTON LOVE, M.D., and JOHN L. JUERGENS, M.D., Mayo Clinic and Foundation, Rochester, Minn. Second thoracic sympathetic ganglionectomy for neurologic and vascular disturbances of the upper extremities. West. J. Surg. 72:130-133, 1964.



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Book Reviews . . .

Coronary Heart Disease: A Personal Clinical Study

by HAROLD FEIL, M.D., *148 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $6.50*

Dr. Feil's monograph is, as he states in his introduction, "a survey of one physician's practice with some references to other authors for the purpose of comparison of data." Very few individuals could write such a book because few would have the years of experience in handling such a large number of cases of coronary heart disease as the 1,854 patients whose histories form the basis for this work.

In this group there were 338 patients with angina pectoris without infarction and 1,516 patients who suffered an infarction. It is remarkable, and an indication of the completeness of Dr. Feil's records and study, that over 90% of these patients were available to follow-up. Throughout the book optimism for the future of the patient with coronary disease is emphasized even though the seriousness of the condition is never underestimated. Dr. Feil points out repeatedly the fact that his experiences over the years justify a reasonably optimistic attitude.

The first chapter describes the anginal patients, the various factors influencing the course of their disease, the complications, and their clinical causes. This is followed by a number of tables setting forth all this material. The next chapter and its subsequent tables similarly present the material on the patients having had a myocardial infarction. The next chapter, similarly set up, compares 2 groups of patients, the first consisting of those having lived twenty years after an infarction and the second consisting of those who lived less than five years after their infarcts occurred. There next follows a number of chapters describing the clinical features, problems in diagnosis, factors determining longevity, and so forth, in patients with angina only and in those with infarcts. Many illustrative cases are interspersed in these chapters.

A brief chapter on the treatment of angina pectoris follows, and this chapter, although very short, is purely practical and to the point. An error in typesetting makes the bottom line of page 128 and the top line of page 129 as well as the first and second lines on page 130 an odd sort of jumble, but this is the only obvious error of this type in the book. It is of interest that in this chapter the author states that intractable angina was "rare" in his practice and usually, when present, "associated with psychogenic factors."

The last chapter entitled "Treatment of Myocardial Infarction" is again written in a most practical manner. Everyone who treats cardiac patients in fairly large numbers doubtless has his own ideas regarding the treatment of patients with acute infarcts, and some of Dr. Feil's general therapeutic measures might not be generally accepted by all cardiologists. One might differ with the author regarding the length of time oxygen is administered. His statement that anticoagulants "are given routinely" would be questioned by some investigators. His initial Coumadin dosage of 60 mg. and cessation of heparin after twenty-four hours do not always fit every case, and more definitive variations in dosages and schedules could have been described. One might also question the need for daily examinations of the urine and stool for evidence of bleeding.

The period of rest is obviously not the same for each case, and Dr. Feil points this out. On the other hand, the generalization for the average case of two weeks of rest following which the patient may walk, and the discharge of the patient from the hospital after about three weeks may be considered too liberal for many cases. He advocates the use of parenteral fluids when the patient is nauseated, but many patients get over their nausea quickly and, unless the nausea is long-lived or dehydration appears, the use of parenteral fluids is not necessary in the opinion of many cardiologists. When such fluids are used, most men would avoid intravenous saline which is suggested by Dr. Feil. The author also advocates the use of an enema if the bowels do not move for four or five days. It would seem that attention would have been directed to this important detail before the passing of four or five days and that mild laxatives would have been given after two, or at most three, days had passed without a bowel movement.

The period of convalescence suggested by the author allows little variability according to the extent of the injury. He states that the patient should not return to work "before the completion of a period of three months following the coronary thrombosis." One is not certain if this means the beginning of return to work or return to full work. Patients with attacks of moderate severity may often start back to limited work after eight or nine weeks.

The author states that atrial fibrillation or flutter is treated with rapid digitalization. He does not mention the fact that many of these arrhythmias are very transitory, reverting to normal sinus rhythm spontaneously, nor does he differentiate between those cases having a rapid ventricular response and those in which the ventricular rate is slow. He also categorically states that 1.2 mg. of digitoxin is the digitalizing dose and 0.1 mg. the maintenance dose, giving no figures for the extremes occasionally required for digitalization and maintenance.

In general the monograph is a most informative review of a very large series of cases of arteriosclerotic heart disease and gives a clear and concise approach to the diagnosis, prognosis, and treatment as evaluated by one of the outstanding cardiologists of our times. It will certainly be of value to all physicians who encounter and treat arteriosclerotic heart disease and is highly recommended for reading and study to all such physicians.

MILTON M. HURWITZ, M.D.
St. Paul

The Thymus

edited by VITTORIO DEFENDI *and* DONALD METCALF, *145 pp., ill., Wistar Institute Press, Philadelphia, 1964. $5*

This monograph is based on a symposium on the thymus gland held at the Wistar Institute on April 29, 1964. The book is composed of papers presented at this symposium by 20 of the participants. Each of the participants is an acknowledged authority in the field of the thymus gland and has presented a summary of the data and conclusions from his work. Each presentation is followed by a dis-

(Continued on page 14A)



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(Continued from page 12A)

cussion of the paper by other participants in the symposium. Most of the papers are well illustrated with tables, graphs, and photomicrographs. Each paper also contains a fairly comprehensive bibliography.

The material presented is primarily basic in nature and particularly pointed toward the immunologic role of the thymus gland. The data presented are almost entirely based on work in experimental animals. The material presented, although quite complex, is clear and understandable to the physician not working in the field. However, the book will be mainly of interest to investigators of immunology and the thymus and also to scientists in related fields. Clinicians will find this material difficult reading. However, if they are willing to spend the time in careful study they will gain a great deal of knowledge of the basic and fundamental functions of the thymus gland. I do not feel that this is a book that a clinician will find useful as a reference or in his practice, but it will make stimulating and interesting reading to supplement his knowledge of current advances in an important area of basic science.

ALVIN L. SCHULTZ, M.D.
Minneapolis

The Mask of Sanity

by HERVEY CLECKLEY, *4th ed., 510 pp., C. V. Mosby Co., St. Louis, 1964. $9.75*

This is a beautiful new edition of a splendid book, which every physician, every sociologist, every criminologist, and every psychiatrist should certainly read. As Dr. Cleckley points out so wisely, there are thousands of men and women—often the children of highly respected people—who are not sensible enough to behave themselves properly. They are always in trouble, often in jail, often in a mental hospital, often uproariously and very offensively drunk, constantly swindling people, or stealing, or obtaining money with bad checks, or doing stupid and mischievous acts which injure their chances of having any success in life. If they steal a car, it is just to drive about in it aimlessly.

As Dr. Cleckley says, they are remarkably alike in their behavior, but occasionally one is found who does not drink. Their crimes are not crimes of passion or great need or violent emotion. Many ruin their careers; they get expelled from college or they lose a good job by stealing a small amount of money that their well-to-do father would gladly have given them. Most of their crimes are petty. Everything they do is rather childish and aimless and without real emotion. Even their sexual life seems to be rather aimless.

These people are often attractive in appearance. When they get caught in some stupid crime, they at first try to lie their way out of it. Often they are very convincing. They so deeply impress people with their great contrition and their determination to mend their ways and go straight that they are paroled. But often that night they wind up in jail.

They have no shame and absolutely no sense of responsibility. They cause their parents or spouse endless trouble and expense and rarely show any real appreciation of what has been done for them. They have no conscience and no desire to take and hold a respected place in the community.

In many ways they obviously are not sane—they cannot behave sanely in their community. Yet when they are put into a mental hospital, they definitely do not be-

(Continued on page 18A)



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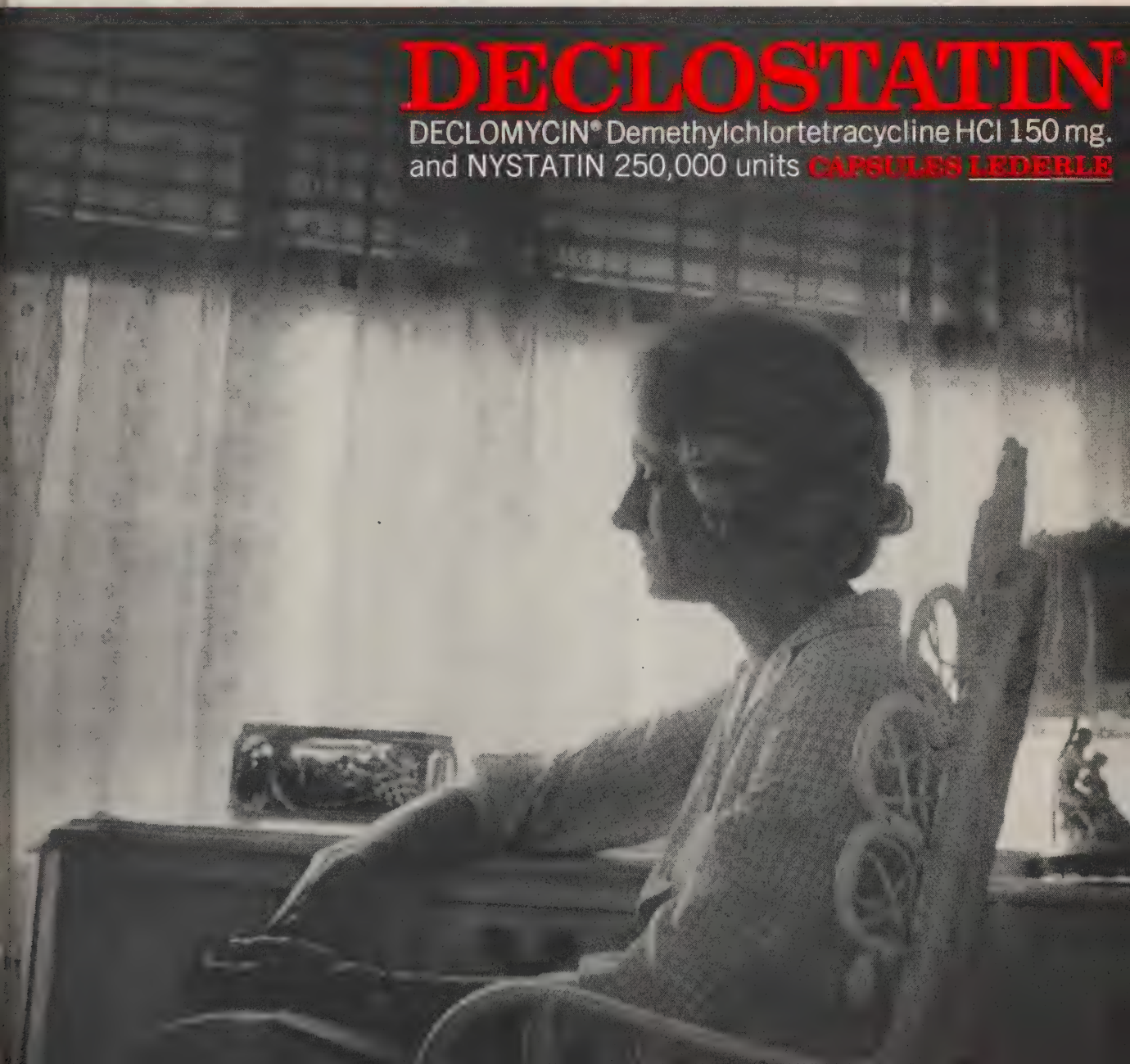
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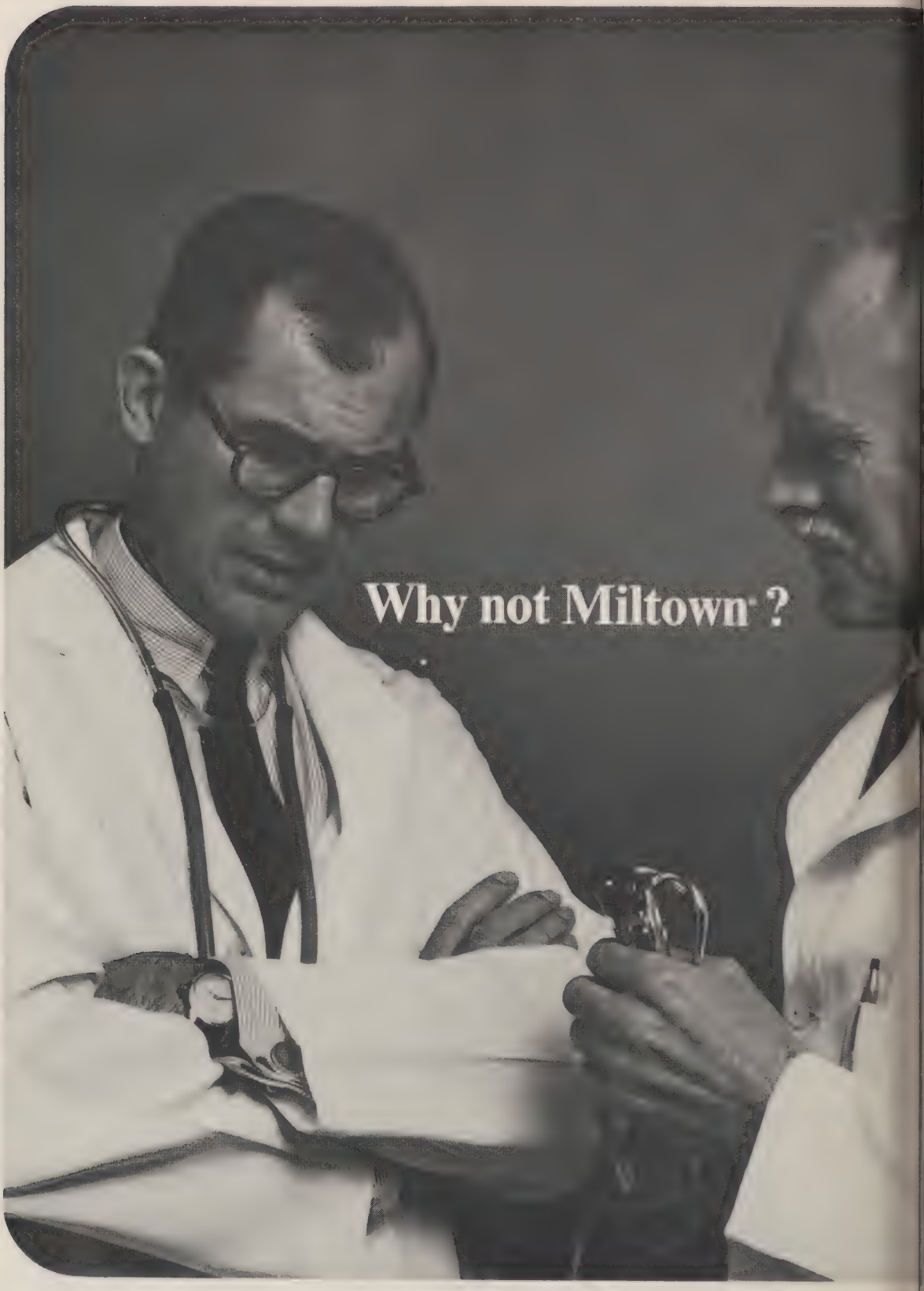
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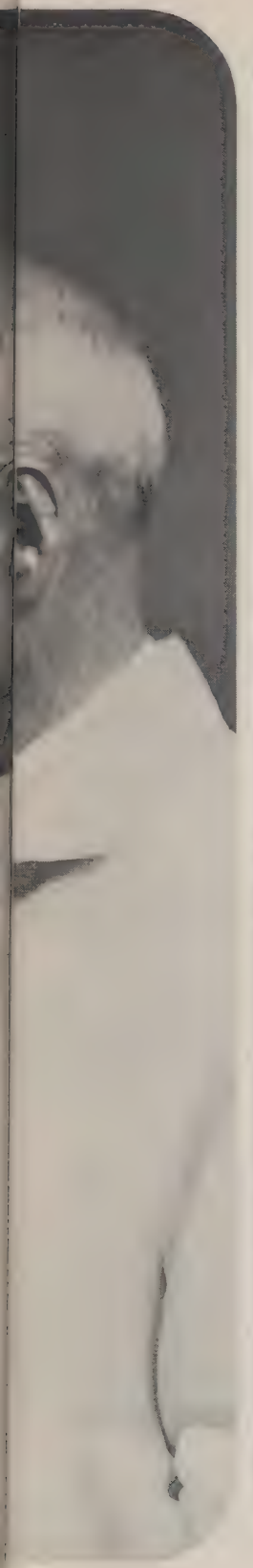
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Precautions: Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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(Continued from page 14A)

long there because they are often very bright, and they argue so sensibly. They have no delusions or hallucinations, and unlike a schizophrenic, they often seem to be very sociable and friendly.

Because they do not fit into any definite group of the insane, they have been largely ignored by psychiatrists and penologists. Some experts say they have a psychopathic personality.

After they have been brought dozens of times into a local court for uproarious drunkenness or petty swindling the judge usually says to the police, "Don't bring that crazy fool in here again; take him to the mental hospital." But there he cannot be held, and hence in a few days he is out again and usually into his old bad habits.

Obviously, society should quickly build some place in which these "crazy" people can be held, perhaps for life, to protect them from their folly; to protect their unhappy families from constant misery and shame and expense; and most important of all, to protect society from the constant depredations of these bad children in adult bodies. It obviously is silly to punish these people, or to treat them, or to parole them, or to keep hoping year after year that they will reform.

Here is a good example of the sort of stupid mischief that these people will get into. During the war, when houses were very difficult to get, while his parents were vacationing, a young man leased his parents' home to an army officer, getting perhaps a couple of months' rent in advance. This money he promptly spent on dissipation in cheap bars and brothels. Imagine a lad doing such a thing, when on his parents' return, they would be horrified, outraged, and caught in a difficult legal situation. Think of the man's lack of shame and lack of concern over the wrath of a father who had been supporting him for years and getting him out of one bad scrape after another.

I think anyone who reads the stories in the first part of this book will agree that these men and women are not sane, in the ordinary layman's sense of the word. But, as Dr. Cleckley says, according to the present-day legal definition of insanity, they are perfectly sane.

My impression is that Dr. Cleckley feels, as I do, that some provision must be made for the classifying of these many people. They behave so much alike that their disease must be a unit and must be due to some definite abnormality of the brain. Penologists must recognize it and must arrange for the care of these people. The judge's idea must not be one of punishment but of protection of the public against the very costly and constant mischief.

Psychiatrists should learn to recognize these people at a glance, and they should agree on a name for their disease.

The ideal thing would be to put all of these people in a big camp or on an island, where they would be treated kindly but firmly. They should be made to work and earn a living for themselves and their dependents.

WALTER C. ALVAREZ, M.D.
Chicago

Heart Attack: New Hope, New Knowledge, New Life

by MYRON PRINZMETAL, *revised edition, 232 pp., ill., Simon and Schuster, New York, 1965. $4.50 cloth, $1.75 paperback*

This book, a second edition, designed for the coronary

(Continued on page 20A)

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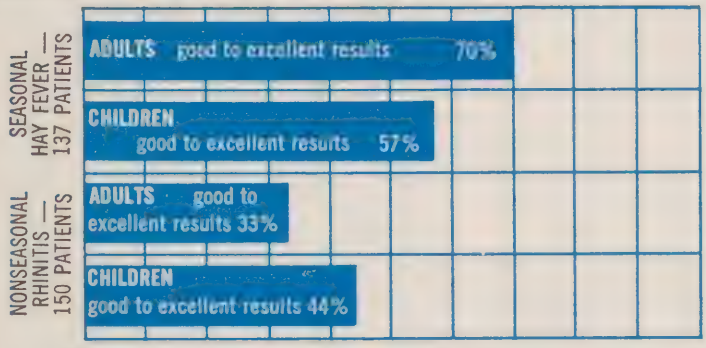
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(Continued from page 18A)

patient is unique in that it is co-authored by a physician and one of his coronary patients. Thus, many of the anxieties and uncertainties felt by the patient can be approached and answered in a manner satisfactory to the layman. It is written in an optimistic style and avoids any "scare" approach. Although it is obvious that the authors have very definite opinions on some of the controversial aspects of the causation, treatment, and prevention of coronary thrombosis, every attempt is made to steer a middle of the road policy and allow reasonable exposition of opposing opinions. Nearly one-third of the narrative portion of the book deals with calories, cholesterol, fats, and weight reduction. The importance of daily exercise is also well explained. The role of tensions and anxieties in this disease is discussed in layman terms and even the subject of sex after an attack deserves a small chapter. The appendix of the book lists calories and fat contents of various foods and offers recipes and diets.

The reviewer recommends this highly for reading by the postcoronary patient but feels that it would be wise for the physician to peruse it also so that he may be better equipped to enlighten his patients when he sees them.

ARTHUR C. KERKHOF, M.D.
Minneapolis

NEW BOOKS RECEIVED

Pediatric Ophthalmology edited by L. BYERLY HOLT, 403 pp., ill., Lea & Febiger, Philadelphia, 1964. $12

Corneal Contact Lenses edited by LOUIS J. GIRARD, 329 pp., ill., C. V. Mosby Co., St. Louis, 1964. $19.75

Handbook of Pediatric Medical Emergencies by ADOLPH G. DE SANCTIS and CHARLES VARGA, 3rd ed., 457 pp., ill., C. V. Mosby Co., St. Louis, 1963. $12.75

Advances in the Treatment of Menstrual Dysfunction edited by ALVIN F. GOLDFARB, 188 pp., ill., Lea & Febiger, Philadelphia, 1964. $4

Disorders of Carbohydrate Metabolism edited by D. A. PYKE, 248 pp., ill., J. B. Lippincott Co., Philadelphia, 1963. $6

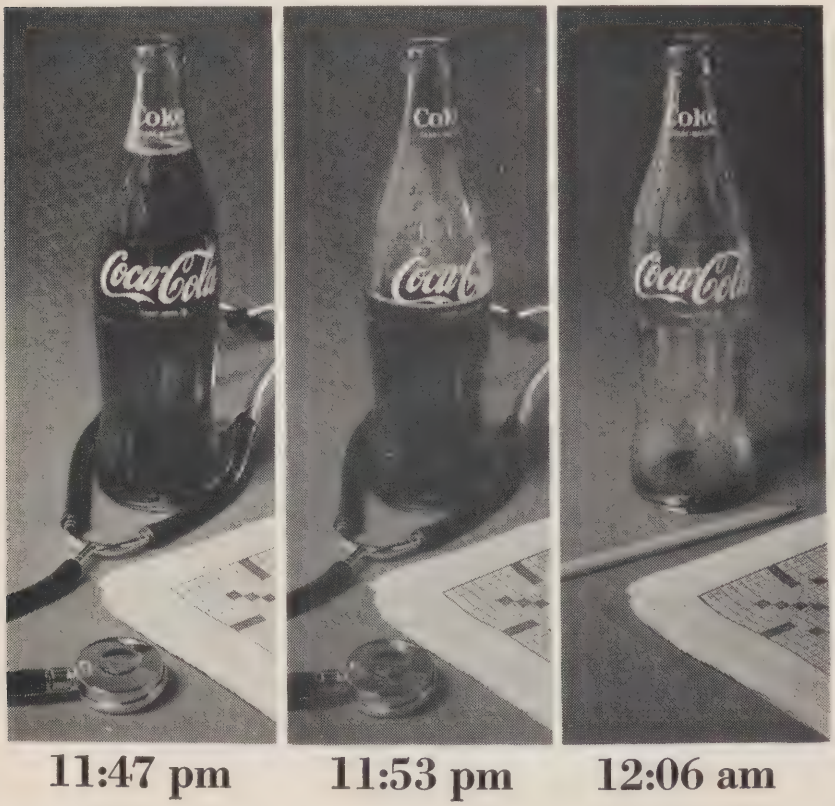
Ocular and Adnexal Tumors: New and Controversial Aspects edited by MILTON BONIUK, 511 pp., ill., C. V. Mosby Co., St. Louis, 1964. $25

How Diabetics Can Eat Wisely by DOROTHY TOMPKINS REVELL, 172 pp., ill., T. S. Denison & Co., Minneapolis, 1964. $3.95

The Structure and Dynamics of Organizations and Groups by ERIC BERNE, 260 pp., ill., J. B. Lippincott Co., Philadelphia, 1963. $7.50

The Visual Fields—A Textbook and Atlas of Clinical Perimetry by DAVID O. HARRINGTON, 2nd ed., 386 pp., ill., C. V. Mosby Co., St. Louis, 1964. $16

Modern Nutrition in Health and Disease edited by MICHAEL G. WOHL and ROBERT S. GOODHART, 3rd ed., 1,282 pp., ill., Lea & Febiger, Philadelphia, 1964. $20



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News Briefs . . .

North Dakota

DRS. PETER R. GREGWARE and CHARLES A. HAMILTON of Bismarck have been inducted as fellows of the American College of Physicians. Both are internists at the Quain and Ramstad Clinic. Dr. Gregware was graduated from Albany Medical College of Union University, N.Y., in 1945, and Dr. Hamilton is a 1953 graduate of Harvard Medical School, Boston.

* * * *

DR. RICHARD A. OLAFSON, who has been a resident in neurological surgery in the Mayo Foundation in Rochester, has moved to Fargo. Dr. Olafson received his medical education at the University of Pennsylvania, Philadelphia, and was graduated in 1959.

* * * *

DR. VICTOR KALJOT, former Army cardiologist, has joined the Northwest Clinic in Minot. A 1955 graduate of the University of Vermont College of Medicine in Burlington, Dr. Kaljot interned at the Mary Fletcher Hospital, Burlington. He is a diplomate of the National Board of Medical Examiners.

Minnesota

DR. RICHARD L. CASTILLO, formerly of Berkeley, Calif., has begun practice in Plainview. Dr. Castillo received his medical education at the University of California School of Medicine and was graduated in 1957.

* * * *

DR. ROBERT R. COOPER of Edina has been elected chief of staff of Fairview Hospital in Minneapolis. Dr. Cooper is a 1946 graduate of the University of Minnesota Medical School and a member of the American Academy of Ophthalmology and Otolaryngology, American College of Surgeons, and Industrial Medical Association. Other officers named were Drs. Meyer S. Belzer, chief-elect; Henry E. Brandt, treasurer; and John A. Hartwig, secretary. Dr. Ralph M. Silas was elected to the executive committee.

* * * *

DR. PHILIP J. PARKER of Staples has announced plans to practice in Fertile with an office in the Vasenden Building. Dr. Parker, a general practitioner and surgeon, was graduated in 1942 from Jefferson Medical College of Philadelphia.

* * * *

DR. CLEON R. HOLLAND of Rochester, a former Mayo Clinic physician, has returned to Rochester State Hospital as a senior staff physician. At one time he was a medical consultant at the hospital. Dr. Holland, a native of Mazeppa, was graduated in 1940 from Hahnemann Medical College, Philadelphia.

* * * *

DR. TERRELL F. YEAGER of Anoka has been installed as a fellow of the American College of Obstetricians and Gynecologists. Dr. Yeager received his medical education at Stritch School of Medicine of Loyola University in Chicago and was graduated in 1956.

* * * *

DR. ROBERT V. HODAPP, Willmar pediatrician, has been appointed for a two-year term on the State Department of Education's Advisory Committee on Health and Physical Education. The committee has been charged with

(Continued on page 22A)

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NEWS BRIEFS

(Continued from page 21A)

the responsibility of studying and making recommendations on certain problems in the field of health and physical education. Dr. Hodapp is a 1946 graduate of the University of Minnesota Medical School.

° ° ° °

DR. E. THEODORE PALM, chief resident in surgery at Swedish Hospital in Minneapolis, was one of the two winners of the $1,000 Ross Awards at the recent annual scientific assembly of the American Academy of General Practice in San Francisco. Dr. Palm received his medical degree in 1946 from the University of Minnesota.

° ° ° °

DRS. EDWARD C. MAEDER and CLARK A. SHATTUCK have announced the opening of a suburban office at 5617 Hampshire Avenue North in Crystal. Practice is limited to obstetrics and gynecology. Both are graduates of the University of Minnesota Medical School, Dr. Maeder in 1927 and Dr. Shattuck in 1958.

° ° ° °

DR. RICHARD R. TEETER has been selected as the new director of psychiatric services at Ancker Hospital in St. Paul and program director of the St. Paul-Ramsey County Mental Health Center. He will take over his new duties in June. Dr. Teeter, a 1947 graduate of the University of Pennsylvania School of Medicine, Philadelphia, is a former Minnesotan and presently psychiatrist and associate professor of psychiatry at Marquette University, Milwaukee.

° ° ° °

DR. JESSE E. EDWARDS, St. Paul, an international authority on heart disease, is the senior author of a new book on congenital heart disease. The book, "Congenital Heart Disease. Correlation of Pathologic Anatomy and Angiocardiography," was published by W. B. Saunders Co. of Philadelphia. Dr. Edwards is director of laboratories at Charles T. Miller Hospital in St. Paul and professor of pathology at the University of Minnesota. One of the coauthors, Dr. Lewis S. Carey, is director of the cardiac diagnostic unit at St. Joseph's Hospital in St. Paul and clinical assistant professor of radiology at the University of Minnesota.

° ° ° °

DR. TRACY E. BARBER, Austin, has been elected secretary of the Industrial Medical Association. Dr. Barber is medical director of George A. Hormel & Co. and a visiting lecturer at the University of Minnesota. He received his medical degree in 1943 from Temple University, Philadelphia, and did postgraduate work at the University of Minnesota.

° ° ° °

DR. LOWELL L. HENDERSON, Mayo Clinic consultant, Rochester, has been named president-elect of the American College of Allergists. He has been a member of the board of regents of the college since 1962 and also served as president of the North Central Allergy Society in 1960-61. Dr. Henderson received his medical degree from Indiana University in 1941.

° ° ° °

DR. BIENVENIDO R. BRIONES, chief resident in the outpatient department at Methodist Hospital, Minneapolis, has joined the Drill Clinic in Hopkins. Dr. Briones, a surgeon and general practitioner, received his medical degree in 1955 at the University of Santo Tomas Faculty of Medicine and Surgery, Manila.

° ° ° °

DR. FREDERICK D. ROTH has been elected president of the Mankato Clinic to succeed Dr. John C. Mickelson. Dr.

NEWS BRIEFS

Roth received his medical degree in 1933 from Marquette University in Milwaukee. Other officers elected were Drs. John J. Heimark, vice-president; Chester E. Thiem, secretary; and Anthony A. Schmitz, treasurer.

* * * *

DR. WILLIAM BRADLEY MARTIN, Duluth heart specialist, has been named chief of cardiology service at the Veterans Administration Center in Dayton, Ohio. Dr. Martin, a native of Knife River, was graduated in 1942 from the University of Minnesota Medical School. He is a member of the American College of Physicians, American Society of Internal Medicine, American Diabetes Association, and American College of Chest Physicians.

* * * *

DR. HARRY F. BISEL, Rochester, has been named head of the section of clinical oncology at Mayo Clinic. He has been with the section since September 1963 as a first assistant. Before coming to Rochester, Dr. Bisel was assistant cancer coordinator at the University of Pittsburgh School of Medicine, where he received his degree in 1942. He is a former president of the American Society of Clinical Oncology.

* * * *

DR. ROBERT D. FEDOR, St. Paul, will join the staff of the Meeker County Memorial Hospital in Litchfield as pathologist on July 1. Formerly associated with the Litchfield Clinic, he has been in residency at the Charles T. Miller Hospital in St. Paul. Dr. Fedor is a 1954 graduate of the University of Minnesota Medical School.

* * * *

DR. CLARK W. TRUESDALE, Glencoe, has been elected president of the Glencoe Municipal Hospital. Dr. Truesdale

(Continued on page 24A)



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WANTED LOCUM TENENS: One month, G.P. or General Surgeon. Minnesota License. Northern Minnesota small town practice. Handsome remuneration. For May, June or July. Reply Box 27, c/o Journal Lancet.

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WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED—General Practitioner in Jamestown, North Dakota. 14 man Multi-specialty group with general practice section. Starting salary $12,000, plus fringe benefits of insurances, vacations, pension plan, time off for post graduate training. Reply to Box 951, Jamestown, North Dakota.

WANTED—Locum tenens—Pediatrician for one year, Multi-specialty group, northern Minnesota. Salary open. Northwestern Clinic, Crookston, Minnesota.

FOR SALE: Expanding busy general practice in heart of Minnesota lake country. New ultramodern hospital. Consultation readily available. Excellent opportunity for Catholic MD. Sell for value of property and equipment. Three bedroom home on shore of beautiful lake available. Reply Box 30, c/o Journel Lancet.

MEDICAL DOCTOR—Medical Technology School desires doctor as a medical advisor. Write or phone Institute of Medical Technique, 1900 LaSalle, Minneapolis—Federal 3-3434.

FOR SALE—General practice, over $50,000 gross, County seat, 40-bed hospital. South Central Minnesota. Equipment for sale, office for lease. Leaving for residency. Reply Box 31 c/o Journal Lancet.

NEWS BRIEFS

(Continued from page 23A)

was graduated from the University of Minnesota Medical School in 1944 and is a member of the American Academy of General Practice. Other officers elected were Drs. John J. Smyth, Lester Prairie, vice-president, and Donald R. Navratil, Glencoe, secretary-treasurer.

South Dakota

DR. ROGER S. JERNSTROM has been installed as a fellow of the American College of Obstetricians and Gynecologists. His late father was a well known Rapid City physician. A 1957 graduate of the University of Utah College of Medicine in Salt Lake City, Dr. Jernstrom has been in practice in Omaha. He also is an instructor at the University of Nebraska.

Deaths . . .

DR. ADOLPH GUSTAV LIEDLOFF, 87, Mankato, died March 20. A lifetime resident of Mankato, Dr. Liedloff entered practice there after graduation from the University of Minnesota Medical School in 1902. He also served as county health officer and coroner.

* * * *

DR. LAWRENCE B. PEARSON, JR., 27, Minneapolis, died April 6. A 1962 graduate of the University of Minnesota Medical School, Dr. Pearson was a staff physician at the Veterans Administration Hospital in Minneapolis.

* * * *

DR. J. STANLEY WELCH, 87, died of a heart attack March 30. A resident of Rochester the last seven years, he formerly was a prominent Lincoln, Nebraska, physician, civic leader, and emeritus professor of surgery at the University of Nebraska. Dr. Welch was a 1903 graduate of Northwestern University Medical School, Chicago.

* * * *

DR. DOROTHY W. HUTCHINSON, 66, Minnetonka, died of a heart attack March 2 while on a vacation in Florida. A staff physician at Glen Lake State Sanatorium since 1930, Dr. Hutchinson was a 1924 graduate of the University of Pittsburgh School of Medicine and a member of the American Thoracic Society.

* * * *

DR. LORAN M. MARTIN, 85, one of the oldest members of the Mayo Graduate School of Medicine Alumni Association, died of heart disease March 26 at his home in Fort Dodge, Iowa. Dr. Martin, who was retired, received his degree in 1903 from Rush Medical College in Chicago.

* * * *

DR. ROLAND EDWARD NUTTING, Duluth pediatrician, died March 26. A native of Clarissa, he was a 1925 graduate of the University of Minnesota Medical School and a member of the Duluth Clinic staff. Dr. Nutting was the first Minnesota state chairman of the Child Health Organization of the American Academy of Pediatrics and a former fellow of the Mayo Graduate School of Medicine of the University of Minnesota.

* * * *

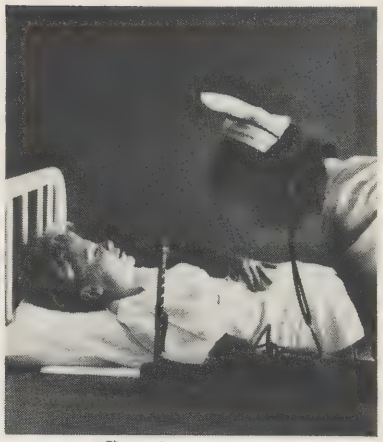
DR. ARTHUR W. GARBRECHT, St. Paul physician, died April 8. A native of Germany, Dr. Garbrecht lived in St. Paul for forty-two years. He was graduated in 1921 from Friedrich-Wilhelms-Universitat Medizinische Fakultat in Berlin and was a member of the Radiological Society of North America.



Edema



Essential hypertension

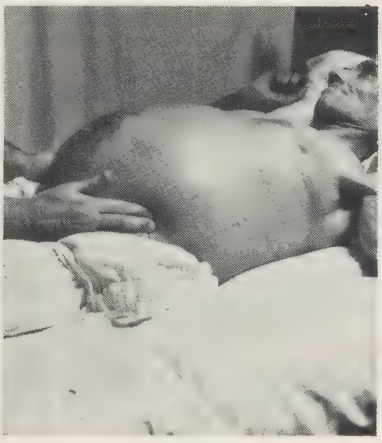


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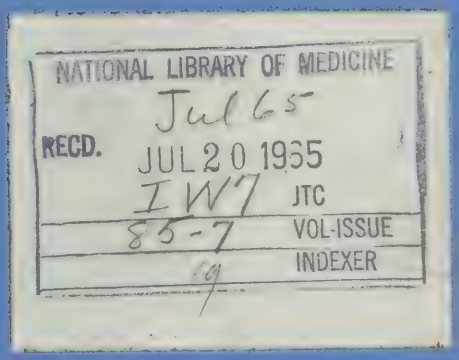
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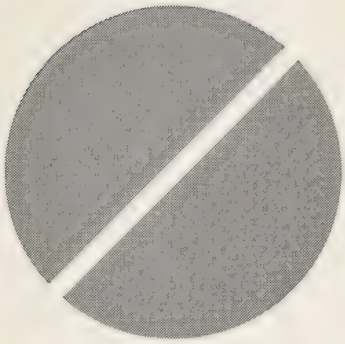
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OFFICIAL JOURNAL, NORTH DAKOTA STATE MEDICAL ASSOCIATION

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JULY 1965





v. 85, no. 7-12
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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, *22*:527, 1964.

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*Pichler, H.: HNO 4:178-179 (May 28) 1954.

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The Journal-Lancet Volume 85, No. 7, JULY 1965

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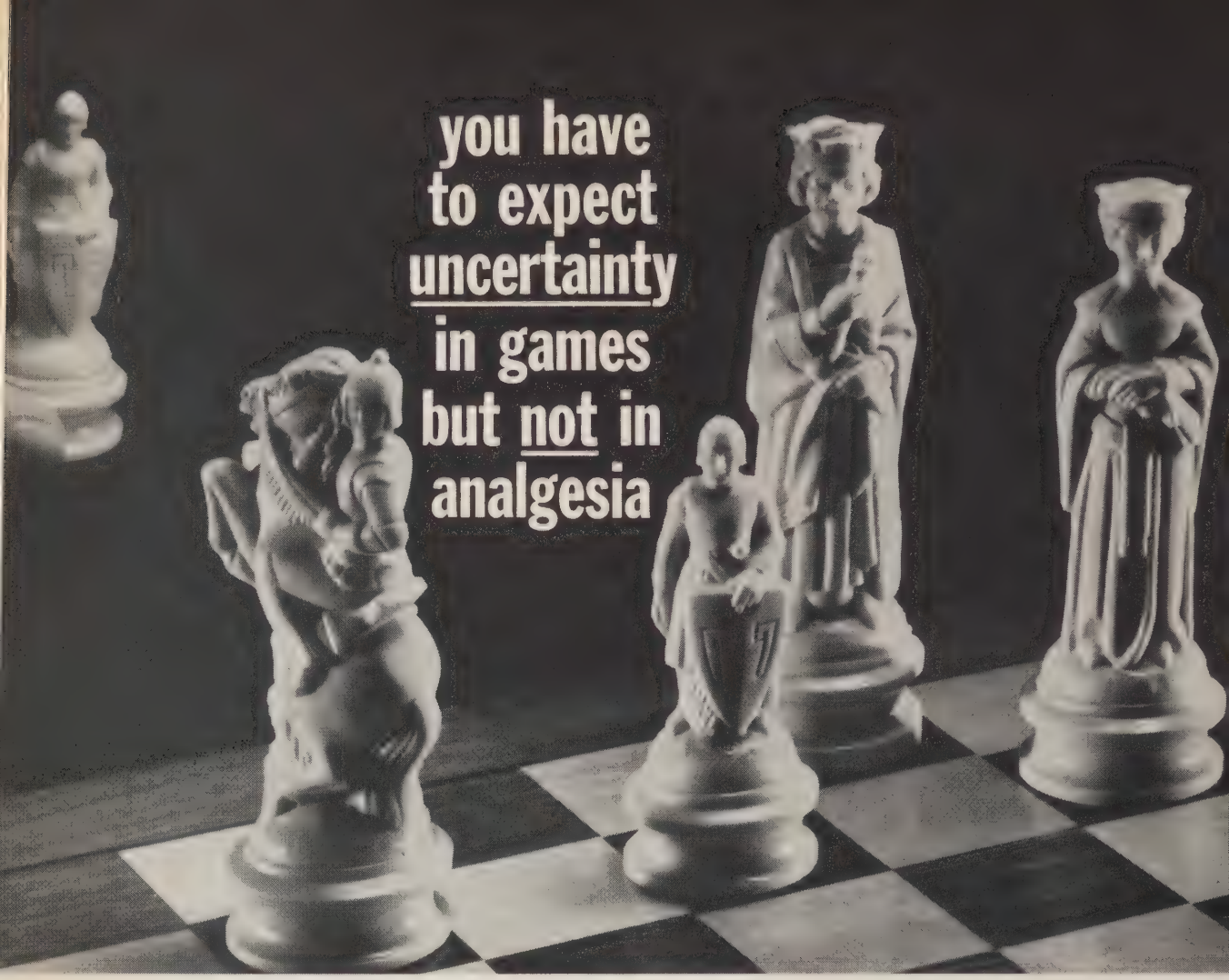
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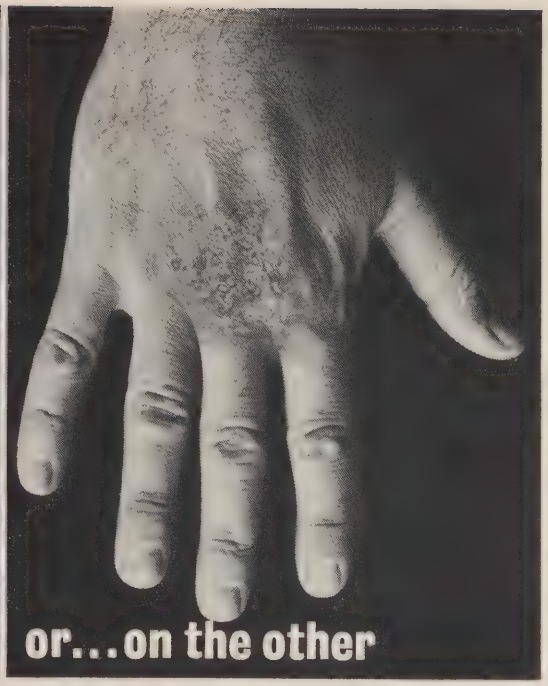
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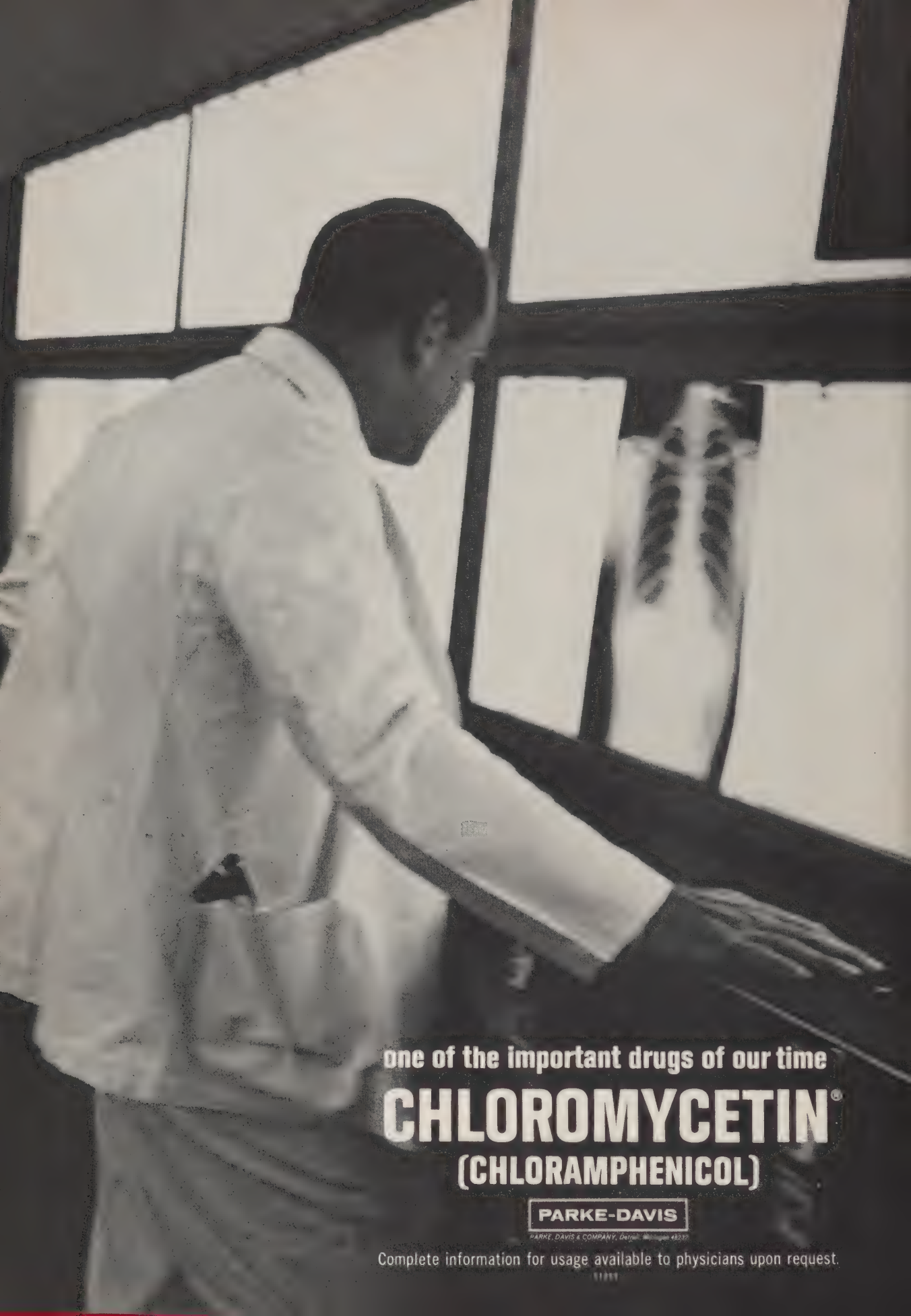
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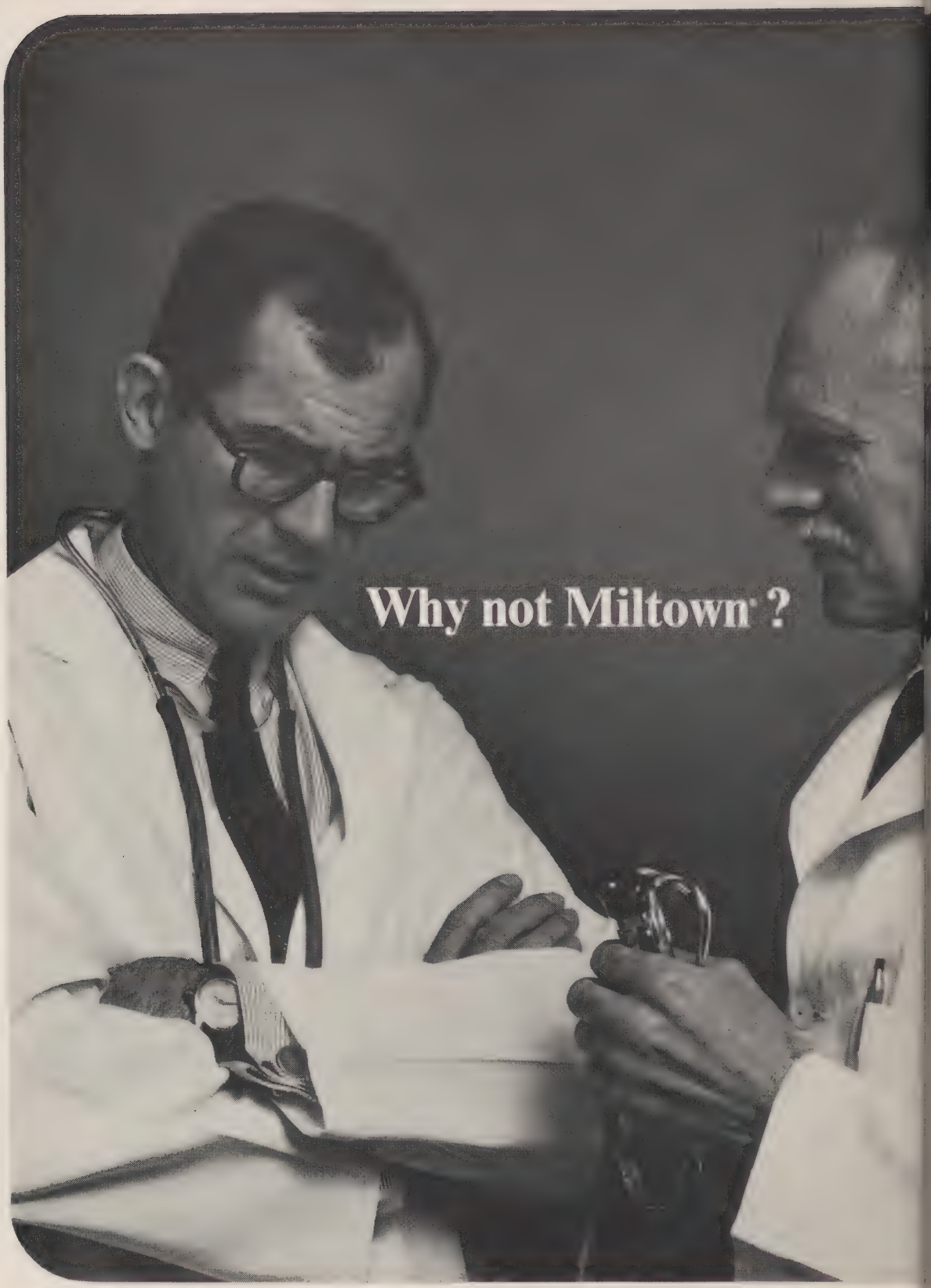
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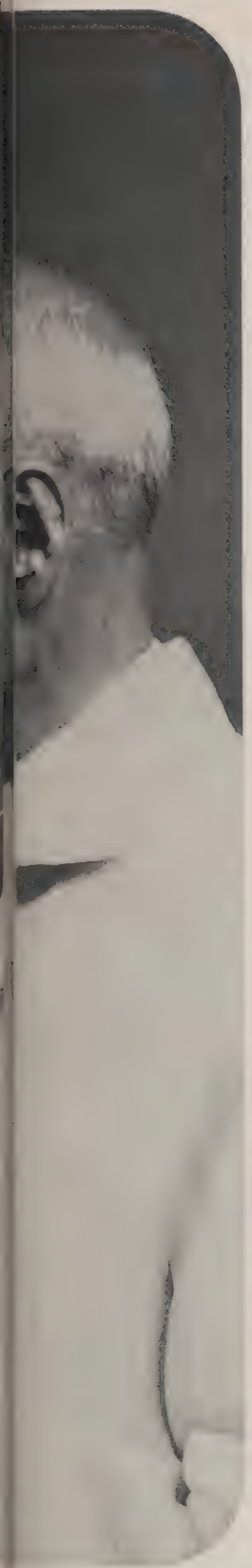
"If we don't think of or look for allergy we will usually fail to diagnose it." So says Kenneth J. Johnson, M.D., of the Quain and Ramstad Clinic, Bismarck, in the leading article, "Fifty Ways to Diagnose Allergy," in the August issue of THE JOURNAL-LANCET. Dr. Johnson has classified 50 items in groups: history and physical findings, cell studies, skin tests, ingestion studies, blood chemistry determinations, serum binding, and therapeutic trials. Conclusive diagnosis should not be made on the basis of only one method; several are necessary.

R. E. Wiederanders, M.D., of Williston, in his article, "Effect of Hydrocortisone on Histamine-Induced Gastric Hypersecretion," reports the results of a study carried out on Heidenhain pouch dogs which indicate that hydrocortisone does not affect histamine hypersecretion, nor does it act as a gastric analogue.

The history of X-ray installations in North Dakota before 1911 is fragmentary. Now, for the first time, all known data have been brought together by H. Milton Berg, M.D., Bismarck, in his scholarly, carefully researched article, "A History of Radiology in North Dakota." Dr. Berg, a past-president of the North American Radiological Society, is planning similar histories for other upper midwest states. The articles will appear in subsequent issues of THE JOURNAL-LANCET.

The second of the new "Series on Neurology for the Practitioner" will be "Disorders of Speech and Language," by A. B. Baker, M.D., director of the Division of Neurology, University of Minnesota Medical School.


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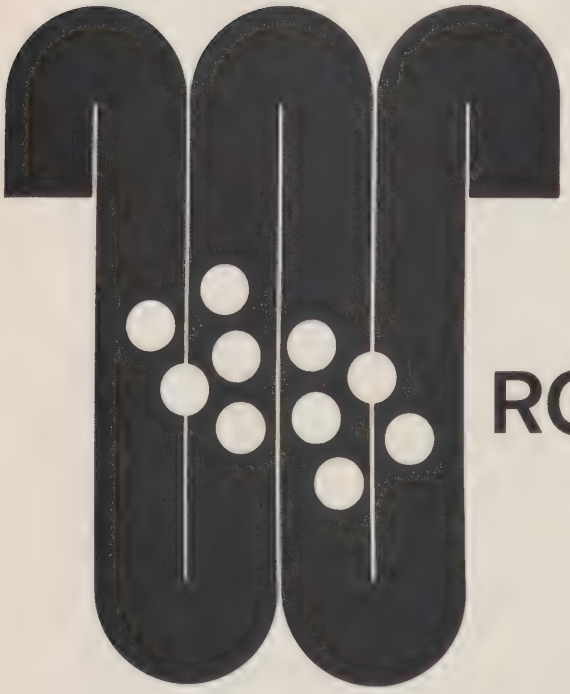
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Spinal Cord Localization

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Minneapolis

LOCALIZATION OF LESIONS within the spinal cord is much easier than within the brain since the neurological systems to be tested are limited in number and readily evaluated. In localizing within the spinal cord, one must consider localization in a longitudinal as well as in transverse planes. Longitudinal localization is used to determine the number of cord segments involved and offers information regarding the extent of the lesion. Transverse localization is used to determine whether the lesion is in the central or peripheral part of the cord, whether it is within or without the cord, or whether it lies dorsally or ventrally.

SYSTEMS USED IN CORD LOCALIZATION

1. *Anterior horn cells.* Involvement of the anterior horns produces weakness, atrophy, and reduced to absent deep reflexes. It is most useful in localizing lesions in the region of the cervical and lumbosacral enlargements which innervate the limbs. Through involvement of the anterior horn cells one can usually localize a lesion accurately to a specific cord segment since each of the muscle groups of the limbs has a specific and consistent innervation from a definite cord segment. It is important that one has a careful knowledge of muscle function, its method of testing, and the cord segment from which these muscles receive their innervation (Fig. 1).

2. *Pyramidal system.* This system is located in the dorsolateral part of the spinal cord and its involvement results in spasticity, hyperactive deep reflexes, clonus, and positive toe signs. Involvement of this system enables one to localize lesions within large regions of the spinal cord rather than to a specific dermatome (Fig. 1). Spasticity of all four limbs indicates a lesion of the high cervical cord while spasticity of only the lower limbs suggests involvement of the lower cervical or the thoracic regions of the spinal cord.

3. *Radicular pain.* Radicular pain offers accurate dermatome localization only early in the disease process. When the pain has been present for a considerable period it becomes diffuse and loses its localizing value.

4. *Superficial sensation.* Impaired superficial sensation occurs through injury to the spinothalamic tract which is situated in the ventrolateral regions of the spinal cord. Involvement of this system is not a good localizing finding particularly for longitudinal localization within the spinal cord. Often in compressive lesions of the spinal cord, the sensory loss will begin well below the level of the lesion and slowly extend upward. Only in severe, complete lesions is there a tendency for the sensory loss to correlate with the level of the lesion.

5. *Deep sensation.* This system is mediated through the posterior columns and consists of position sense, muscle and tendon pain, vibration

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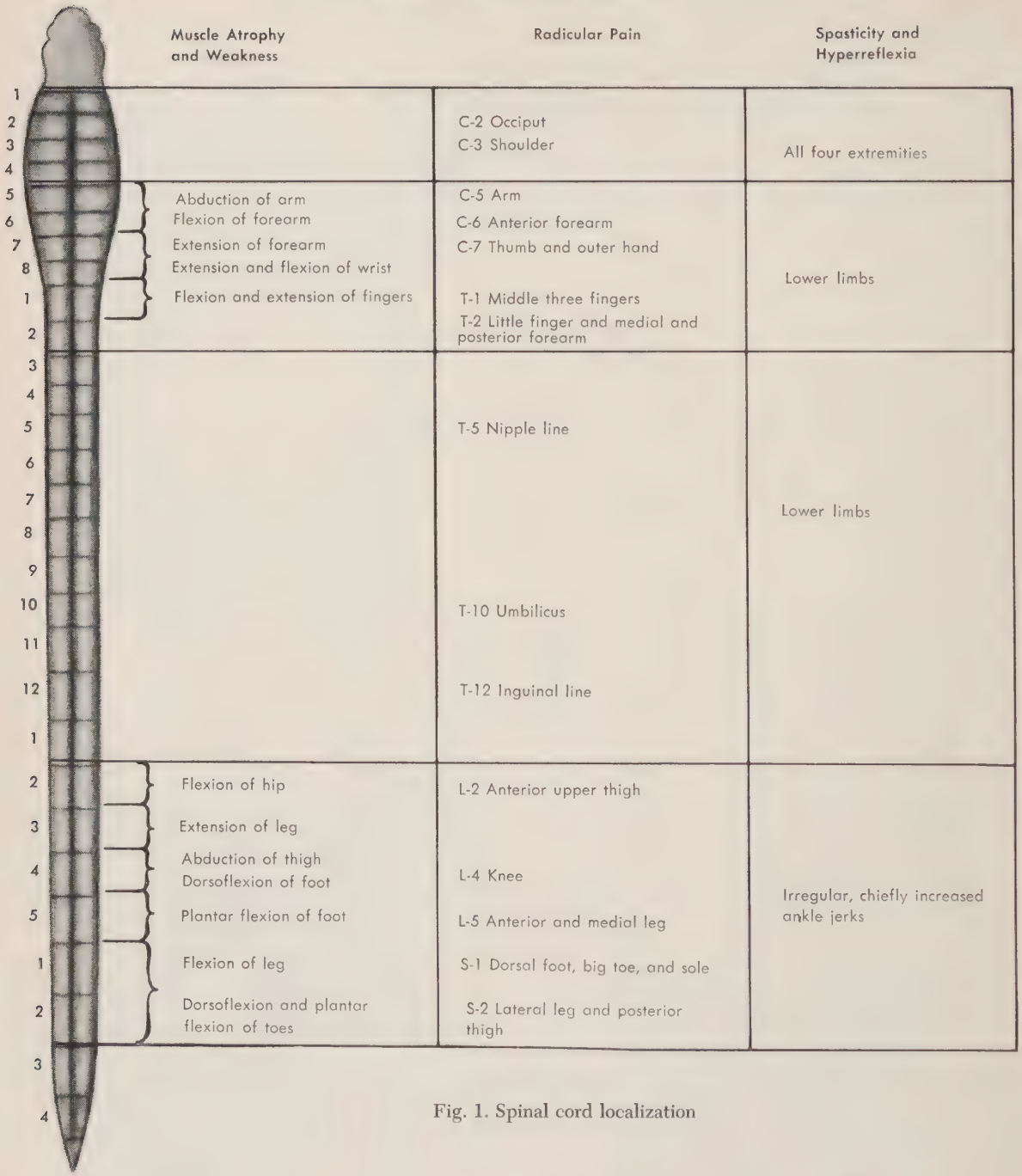


Fig. 1. Spinal cord localization

sense, and testicular pain. In the usual neurological examination deep sensation is tested only in the lower limbs, suggesting that its value is only in transverse localization within the spinal cord. No attempt is made to use deep sensation in longitudinal spinal cord localization.

LONGITUDINAL SPINAL CORD LOCALIZATION

From the point of view of clinical symptomatology, the spinal cord longitudinally can be divided into five different segments, each of which presents a distinct group of clinical manifestations (Fig. 1).

Segment I. This segment extends from the second to the fourth cervical segments of the spinal cord (C_2-C_4).

Motor involvement: Spasticity and increased

deep reflexes will be present in all 4 limbs.

Muscle weakness will be present only in raising the arm above the horizontal due to involvement of the upper trapezius muscle.

Sensory involvement: Radicular pain will extend to the occiput if the C_{2-3} segments are implicated, and to the shoulder if the C_{3-4} segments are involved.

Segment II. This segment extends from the fifth cervical cord segment to the second throacic segment (C_5-T_2, Fig. 1).

Motor involvement: Spasticity and increased deep reflexes will be present in the lower limbs only.

Muscle weakness and atrophy will depend upon which cord segments are involved. Involvement of the following spinal cord segments causes the most clearly defined disturbances:

1. C_{5-6}: Disturbances in abduction and supination of the arm and flexion of the elbow due to involvement of the biceps, deltoid, and supinator muscles

2. C_{5-8}: In addition to the above there will be impaired internal rotation and adduction of the arm.

3. C_{7-8}: Produces weakness in extension of the arm at the elbow as well as impairment in flexion and extension of the wrist.

4. C_8-T_1: Interferes with flexion of the digits on making a fist.

Sensory involvement: Sensory disturbances or radicular pain involves fairly specific areas of the upper limb depending upon the cord segment implicated. The following is a practical guide to such disturbances: (1) cervical five (C_5), the arm; cervical six (C_6), the anterior forearm; cervical seven (C_7), the thumb and outer hand; cervical eight (C_8), the middle fingers and adjacent hand; thoracic one (T_1), the little finger and the entire medial arm and forearm.

Segment III. This segment extends from the second thoracic to the second lumbar cord segments (T_2 to L_2). This area of the spinal cord presents very few clinical findings and accurate localization within this area is somewhat difficult and often not too accurate.

Motor involvement: Characteristically the patient presents with a spastic paraplegia, and isolated muscle weakness does not occur since the abdominal and spinal muscles are innervated by numerous spinal cord segments and are not involved by isolated lesions of this area of the spinal cord.

Testing for the abdominal reflexes may offer some localizing help provided there is a selective disappearance of these reflexes. Complete absence of the abdominal reflexes has no localizing value. Absence of the upper abdominal reflexes points to a lesion of the seventh to the ninth cord segment (T_{7-9}). If the middle abdominal reflexes are also absent the lesion is lower at the ninth to the eleventh thoracic cord segment (T_{9-11}). The lower abdominal reflexes are usually innervated by the eleventh and twelfth thoracic cord segments (T_{11-12}).

Sensory involvement: There are three gross landmarks for the localization of radicular pain and sensory disturbances in this area of the spinal cord. The fifth thoracic segment is usually related to the nipple level, the tenth thoracic level to the umbilicus, and the twelfth thoracic level to the inguinal region.

Segment IV. This segment extends from the second lumbar to the second sacral cord segments (L_2-S_2). It innervates the lower extremity (Fig. 1).

Motor involvement: Generally there is no spasticity of the muscles of the legs. However, if the upper lumbar segments are involved, the ankle jerks may be brisk with ankle clonus and positive toe signs. These disappear when the lower lumbar and upper sacral cord segments are implicated.

Muscle weakness and atrophy will depend upon the spinal cord segments involved. Involvement of certain cord segments in this area offers very specific and easily detectable muscle weakness such as:

1. L_2: Results in impaired flexion of the hip on the abdomen and produces great difficulty in walking because of an inability to raise the leg

2. L_3: Produces impaired extension of the knee due to weakness of the quadriceps muscle. This interferes with standing and the patient will complain of sudden falling without cause.

3. L_{2-3}: In addition to the above disturbances, involvement of these two cord segments produces a weakness of adduction of the hip.

4. L_{4-5}: Such a lesion results in difficulty in abduction of the hip as well as of dorsiflexion and eversion of the foot. The latter is due to peroneal nerve weakness and produces the easily recognizable foot drop.

5. L_5-S_1: This segment innervates the gastrocnemius muscle causing plantar flexion of the foot. Its involvement prevents the patient from walking on his toes.

6. S_{1-2}: Produces involvement of the hamstring muscles with disability in flexion of the knee

7. S_1: Produces impaired dorsiflexion of toes,

while S_2 results in impaired plantar flexion of toes.

Sensory involvement: Sensory disturbances or radicular pain is fairly accurately localized to specific areas of the lower extremity. The following is a crude guide to such localization: Lumbar two (L_2), anterior upper thigh; lumbar three (L_3), anterior lower thigh; lumbar four (L_4), anterior and medial leg; lumbar five (L_5), dorsal aspect of foot and big toe; sacral one (S_1), plantar surface of foot; sacral two (S_2), lateral aspect of leg and posterior aspect of thigh.

Segment V. This area comprises the lower three sacral segments and the coccygeal segment of the spinal cord and is called the conus medullaris. Involvement of this portion of the spinal cord gives rise to some highly characteristic signs such as: (1) paralytic incontinence with a distended bladder, (2) fecal incontinence often followed by constipation, (3) impotence, (4) perianogenital or "saddle" sensory loss, and (5) absence of any motor disturbances in lower limbs since the lower limbs derive their motor innervation from the spinal segments above the conus.

Owing to the fact that there is a differential growth between the vertebral column and spinal cord, the latter terminates at about the first lumbar spinal column level. From this point the spinal roots descend to their respective intervertebral foramina which lie at a level below the spinal cord. The spinal canal, therefore, alongside and below the conus is filled with these descending roots which are referred to as the cauda equina. The relationship between the conus and cauda often makes precise differentiation between lesions of these two structures difficult. Thus compression of the cauda equina at the L_{3-4} level may give rise to the same findings as lesions of the conus. Usually, however, lesions of conus are symmetrical while cauda lesions often predominate on one side. Conus lesions rarely produce spontaneous pain while cauda lesions often give pain referred to the perineum, over the sacrum, and to the bladder.

TRANSVERSE CORD LOCALIZATION

Many of the functional systems within the spinal cord are characteristically involved in different disease processes. These characteristic patterns of spinal cord involvement have been referred to as spinal cord syndromes. They refer only to the anatomic involvement of the spinal cord. There is often a specific group of clinical diseases which should be considered whenever these syndromes are encountered.

Subacute combined syndrome (Fig. 2A): There is an involvement of the posterior and lateral columns of the spinal cord resulting in impaired deep sensation and spasticity of the involved limbs. This syndrome manifests itself in a gait disturbance, the nature of which will depend upon which of the traits are predominantly involved. In most cases the pyramidal system is chiefly implicated producing bilateral spasticity in the legs which is manifested by a slowing of gait and a great difficulty in walking downstairs. If the posterior columns are also severely involved the gait may also be somewhat ataxic.

Many intrinsic as well as extrinsic conditions may produce this syndrome. Among the diagnostic possibilities one should consider the following: nutritional factors as pernicious anemia, malabsorption syndromes, alcoholism, beri-beri, intoxications chiefly with heavy metals, infections as taboparesis, and extramedullary compressive lesions.

Tabetic syndrome (Fig. 2B): In this condition the involvement is limited to the posterior columns of the spinal cord resulting in impaired position and vibration sense with decreased muscle and tendon pain. Clinically, the patient shows an increased gait difficulty due to incoordination. Early this gait difficulty can be compensated for by the use of the eyes, so that there is greater difficulty in walking in the dark.

A number of diseases must be considered when a patient presents with primary posterior column disease. The most common one is tabes dorsalis in which the ataxic gait is often accompanied by the other findings of the luetic involvement. The other conditions that must be considered are early subacute combined degeneration due to pernicious anemia, as well as extramedullary compressive lesions of the spinal cord.

Amyotrophic lateral sclerosis syndrome (combined motor system disease, Fig. 2C): In this syndrome there is an involvement of the anterior horn cells and the pyramidal system producing clinically weakness, atrophy, and fasciculations of the involved musculature associated with hyperactive reflexes and positive toe signs. The muscular weakness may implicate any muscle group including those supplied by the cranial nerves often resulting in bulbar palsy with nasal speech and difficulty in swallowing.

The most common entity producing this combined motor system disease is amyotrophic lateral sclerosis which affects elderly individuals and has a rapidly progressive course resulting fatally in about two years. In the elderly, cervical osteoarthritis may produce a hypertrophic bony bar which can compress the spinal cord and result in this syndrome. In these patients, however,

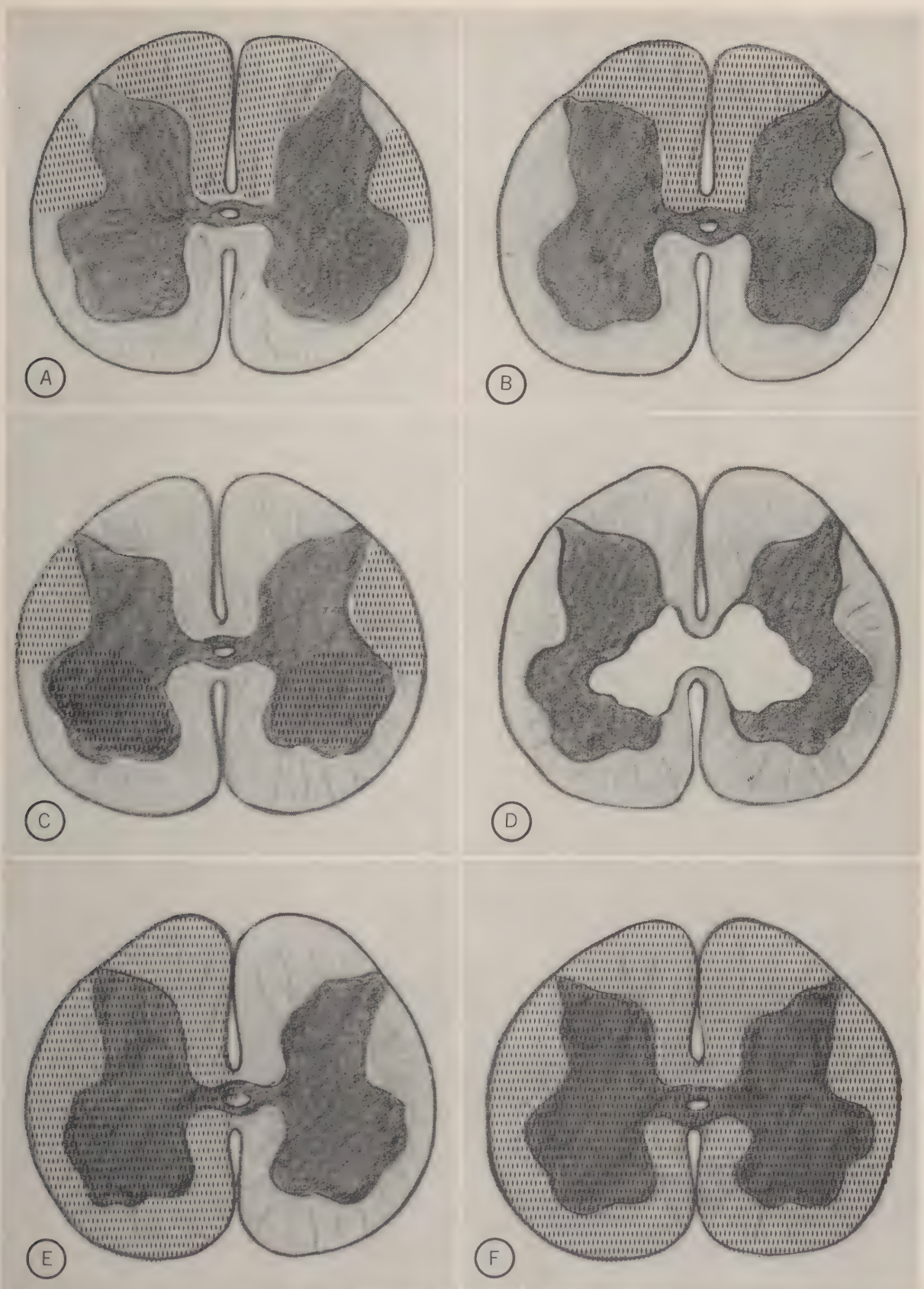


Fig. 2. Spinal cord syndromes, (A) subacute combined syndrome, (B) tabetic syndrome, (C) amyotrophic lateral sclerosis syndrome, (D) syringomyelic syndrome, (E) Brown-Séquard syndrome, and (F) transverse myelitic syndrome

there is often radicular pain in the upper limbs and the weakness and fasciculations tend to predominate in the upper extremities. Toxines such as mercury poisoning may also injure the motor systems of the cord and produce this syndrome.

Syringomyelic syndrome (Fig. 2D): This syndrome results from an involvement of the center of the spinal cord. Clinically there is a segmental loss of pain and temperature with intact light touch (dissociated sensory loss). Often, in addition to this unusual sensory impairment, there is an associated pyramidal tract involvement below the lesion with spasticity and positive toe signs.

Syringomyelia is the most common cause of this syndrome. This consists of a degenerative cavitation of the spinal cord. It occurs chiefly in the cervical and upper thoracic cord levels, manifesting itself in a slowly progressive course. At the onset there usually is some weakness and atrophy of the hand muscles later accompanied by spasticity of the legs, a Horner's syndrome, and Charcot joints in the upper limbs, as well as the classical dissociated sensory loss. Intramedullary spinal cord tumors such as an astrocytoma or an ependymoma may produce a similar clinical picture. Here, however, the lesion is not limited to the upper cord levels and the clinical findings are somewhat more irregular. Hematomyelia or hemorrhage into the spinal cord usually has a more acute onset often associated with pain. Its course is usually one of improvement rather than progression.

Brown-Séquard syndrome (Fig. 2E): In this syndrome there is a unilateral destruction of the cord usually caused by some external process such as a stab wound or by unilateral pressure from a tumor mass.

Clinically the findings are very characteristic and consist of: (1) ipsilateral loss of deep sensation, position sense, and muscle tendon pain below the level of the lesion, (2) ipsilateral spasticity and increased deep reflexes below the lesion, (3) ipsilateral segmental muscle weakness at the level of the lesion, and (4) contralateral loss of superficial sensation, pain, and temperature, below the level of the lesion due to the crossing of this system as it enters the spinal cord.

Transverse myelitic syndrome (Fig. 2F): In this syndrome all the systems tested in the spinal cord are bilaterally implicated. This syndrome is usually caused by external compression of the spinal cord by missile wounds, compression by bony changes, or compression by tumor.

Often one encounters difficulty in determining whether the spinal cord has been completely or only partially injured. This may become a very important decision in spinal cord injuries since the prognosis for recovery will depend upon the completeness of the cord damage. Some rough guidelines, therefore, may prove helpful.

An incomplete cord compression produces: (1) paraplegia-in-extension, (2) paralysis which is not symmetrical, (3) a variable area of anesthesia which is not consistent with the motor loss, and (4) a two-phase flexor, withdrawal reflex in which the stimulated leg will contract and return to its original extended position.

A complete cord transection results in: (1) paraplegia-in-flexion, (2) symmetrical motor paralysis which is consistent with the sensory loss, (3) vasomotor and sphincter changes, and (4) a one-stage flexor-withdrawal reflex in which the stimulated limb withdraws but does not return to its original position.

COMMON BILE DUCT EXPLORATION during cholecystectomy is advisable, since little risk is added and incidence of choledocholithiasis and frequency of choledochotomy increase with age. The chance of stones in the common duct is greater among elderly persons because they probably have had gallstones for a prolonged period. Most patients with gallstones are women. Incidence in men rises with age from less than 30% among those younger than 40 years to more than 40% in those 60 years or older. Although still an indication for exploration, the common duct is dilated in many patients who do not have choledocholithiasis, but many patients with choledocholithiasis do not have recognizable dilation. Jaundice in the immediate preoperative period increases chance of choledocholithiasis more than only a history of jaundice. The common duct was explored surgically in 1,127 patients undergoing cholecystectomy for cholelithiasis. Choledocholithiasis was discovered in 42.6%.

ROBERT M. APPLEMAN, M.D., JAMES T. PRIESTLY, M.D., and ROBERT P. GAGE (deceased), M.S., Mayo Clinic and Foundation, Rochester, Minn. Cholelithiasis and choledocholithiasis: Factors that influence relative incidence. Mayo Clin. Proc. 39:473-479, 1964.

Mesodermal Mixed Tumors

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THE PROGNOSIS in mesodermal mixed tumors of the uterus is very poor. In 1893 Von Franqu[1] reported 1 patient who survived longer than ten years. Hartfall, in 1931,[2] reported 1 five-year cure. Glass and Goldsmith,[3] in 1941, reviewed 94 patients and stated that "the average duration of life following removal is one year." The same year Lebowich and Ehrlich,[4] reporting 13 patients, including their own, said the longest survival rate was four and one-half years. In 1951 Hill and Miller[5] stated that no five-year survivals had been recorded. Most of Ober and Edgecombs'[6] 10 patients in 1954 had died before twenty-six months. Sternberg, Clark, and Smith,[7] that same year, reported their 21 patients as having an average survival rate from the date of onset of symptoms as 11.7 months; from the date of definitive diagnosis, 8.4 months. Symmonds and Dockerty,[8] in 1955, reported 19 patients of which 4 were living from nine to nineteen years later. They stated at that time that the literature revealed only 3 patients surviving longer than five years.

It seems, therefore, worthwhile to report individual patients with long survival histories. The case here presented has survived at present writing, January 1965, more than eight years from the onset of symptoms and is in excellent health.

CASE REPORT

A 40-year-old patient was referred to me in September 1956, because of multiple uterine fibroids associated with menorrhagia and metrorrhagia. Her past history was comparatively normal. She had had 3 normal pregnancies. She had experienced mild secondary anemia on several previous occasions. Otherwise, she had been well until August of 1956 when she noted excessive uterine bleeding. Examination had shown multiple small fibroids in the corpus of the uterus and a fibroid in the anterior portion of the cervix. At the time of admission she had no complaints except the above noted menorrhagia. Her gastrointestinal, genitourinary, and cardiorespiratory history was normal. There was no family history of cancer, diabetes, tuberculosis, or hypertension.

Examination showed a well developed and nourished woman in no acute distress. Her temperature was normal; blood pressure was 160/100. Both head and throat were normal. The neck was normal with no thyroid enlargement. Breasts, heart, and lungs were normal. The abdomen showed no abnormalities, masses, spasm, or tenderness. Pelvic examination showed good anterior and posterior support. There was a nodule palpable in the anterior portion of the uterus at its junction with the cervix. The vagina was clear; the cervix itself appeared normal. There were numerous nodules palpable in the fundus of the uterus. The ovaries and adnexa appeared to be normal. Rectal examination was normal and the extremities were normal. The urine was normal. Hemoglobin was 12 gm. Blood urea was 36 mg. percent. X-ray of the chest was normal except for obliteration of the left costophrenic sinus by old pleural thickening. The electrocardiogram was normal.

On Sept. 18, 1956, a total abdominal hysterectomy, left salpingo-oophorectomy, and incidental appendectomy were done. Exploration of the abdominal cavity showed no abnormality, except for the uterus which was moderately enlarged and showed numerous small fibroids in the lower portion of the corpus and about the proximal portion of the cervix. There was a 6 cm. serous cyst in the left ovary. The right ovary was normal. The patient made an uneventful postoperative recovery and was discharged from the hospital on the tenth postoperative day in good condition. The diagnosis was fibromyoma uteri. Pathological examination of the removed specimens showed no evidence of malignancy in the uterus. The cervical mucosa was eroded and the fibroids appeared to be benign fibromyomata.

A month later there was noted to be a small

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amount of granulation tissue on the vault of the vagina which was cauterized with silver nitrate and gradually disappeared. During the next few years the patient got along well except for gradually increasing symptoms of menopause which were controlled with conjugated estrogens (Premarin®) and mild sedation. Her blood pressure was usually in the range of 140 to 150 systolic and 70 to 80 diastolic, but occasionally blood pressures of 170/100 were noted. In December of 1961, because of complaints of lassitude and fatigue, she was placed on small doses of thyroid. Pelvic examination in December 1960 was normal.

In October 1962 she was seen on the medical service complaining of headaches, particularly occipital headaches, and occasional nausea. She also complained of low back pain and urinary frequency. Her headaches had been very severe and had not responded to mild analgesics from her local doctor. For several weeks she noted urinary frequency and occasional slight blood in the urine.

On examination she looked chronically ill and nervous. Her blood pressure was 184/134. Her pulse was 80. The temperature was normal. She weighed 125 lb. Her nose and throat showed some postnasal discharge and pallor of the mucous membranes. The heart and lungs were normal. Examination of the abdomen showed an indefinite fullness in the lower abdomen, but no definite masses. The breasts were normal. Pelvic examination showed fixation of the vagina on all sides with a hard, nontender, indurated mass. Extremities were normal. Tendon reflexes were normal. Urinalysis showed trace of albumin and occasional white blood cells. Hemoglobin was 10.8 gm. and the leukocyte count was 8,400.

The patient was thought to have a metastatic pelvic carcinoma and was admitted to the hospital for study. The blood urea was 70 mg. percent. An intravenous pyelogram showed good function on the right kidney but no function on the left. The retrograde pyelogram and cystoscopy confirmed the normal kidney on the right. The left ureter could not be catheterized. Pelvic examination under general anesthesia showed a tumor involving the rectovaginal septum, more marked on the left and extending into the left pelvis. At the time of bimanual examination under anesthesia, it was possible to feel the upper portion of a mass and outline it clearly. There was marked fixation in the pelvis especially in the left area of the trigone.

A punch biopsy of the indurated area showed granulation tissue and mucosa. Therefore, under general anesthesia the mucosa over the mass was incised and a wedge segment of tissue was removed. This was reported to be mesodermal mixed tumor. The pathologist then reviewed the sections of the uterus removed in September 1956 and found 1 fragment of tissue which had a small area of cervical mucosa at one edge, beneath which there was a myxomatous tumor with the appearance of neoplastic process. It was believed to be a mesodermal mixed tumor.

X-rays of the chest, stomach, colon, and bones showed no evidence of metastasis, and exploratory laparotomy was determined upon. During surgery the upper abdomen was found to be entirely normal. In the pelvis the distal sigmoid was found to be securely attached to a firm, fixed, and stony hard mass extending out from the area of the posterior portion of the bladder and trigone to the pelvic wall. The right kidney was normal. The left was small and atrophic. Definitive treatment was decided against and the abdomen was closed. The patient made an uncomplicated postoperative recovery and subsequently was treated with a course of cobalt therapy. She was given a total dose to midpelvis of 4366 r. The patient tolerated the therapy well. At the completion of therapy her hemoglobin was 10.7 gm., the white blood count was 6,700, and the blood urea was 28 mg. percent.

In February 1963, pelvic examination showed marked diminution of the mass in the pelvis. The patient at this time was completely comfortable and her general condition was excellent except that her hemoglobin was 9.7 gm. When seen again in March 1963, pelvic examination showed slight bilateral induration in the region of the upper vagina but the previously noted mass had entirely disappeared. The rectal wall was soft and no mass was palpable rectally. X-ray of the spine was taken because of slight pain in the right sacroiliac area. This X-ray, as well as the X-ray of the chest, was negative. Hemoglobin was 10.8 gm.

When last seen in June 1963, the patient was well except for moderate low back pain. She was holding her weight well and her general condition was good. Pelvic examination showed some induration in the lateral vaults, but no definite tumor was palpable and the vagina was more mobile than it had been previously. The hemoglobin was 12 gm., the white blood count was 5,100, and the blood urea was 48 mg. percent.

DISCUSSION

Mesodermal mixed tumors can be defined as tumors composed of a variety of types of mesodermal tissue thought to arise from mesenchymatous tissue representing 1 germ layer.

A review of the literature will quickly reveal that there is no general agreement on classification of these tumors or on criteria for their recognition. This is evidenced in part by the many names under which they are described, for example, sarcoma botryoides, carcinosarcoma, or rhabdomyosarcoma. Much of the confusion arises from the fact that it may be difficult to differentiate between the unusual sarcoma and the mixed mesodermal tumor. Since a tumor is often named according to the predominant element of its heterologous tissue, a tumor composed almost completely of myxomatous tissue might be classified as a myxosarcoma; one composed almost completely of fibrous tissue might be classified as a fibrosarcoma; and one almost completely composed of striated muscle might be called a rhabdomyosarcoma, although a prolonged search with varied types of stains might demonstrate other elements such as cartilage or rhabdomyoblasts, either striated or granular. McFarland,[9] after an extensive study of mixed tumors of mesodermal origin, felt that undue prominence of 1 element should not give its name to a whole growth.

Pack[10] classifies sarcomas of the uterus as, first, pure homologous tumors such as endometrial stromal sarcoma composed of cells ordinarily found in the uterus; second, pure heterologous tumors such as rhabdomyosarcoma, chondrosarcoma, and osteosarcoma composed of cells not normally found in the uterus; and third, mixed sarcomas such as carcinosarcoma, mixed mesenchymal sarcomas, and sarcoma botryoides, all of which contain an admixture of elements and comprise 60% of the mesenchymal sarcomas. Symmonds and Dockerty[8] call a tumor with heterologous elements mesodermal mixed tumor, and Ober[6] calls such a tumor a mesenchymal sarcoma.

Sternberg, Clark, and Smith[7] believe that malignant mixed müllerian tumor is a better designation than mixed mesodermal tumor, and point out that carcinomatous elements occur in various admixtures but are limited to the histological type ordinarily seen in the endometrium, cervix, fallopian tube, or vagina. The connective tissue components have specific and broader capacity for sarcomatous differentiation and admixtures of rhabdomyosarcoma, chondrosarcoma, leiomyosarcoma, or malignant lymphoma may be present. The restricted range of carcinomatous differentiation characterizes the neoplasms as fundamentally müllerian and separates them from true teratoma.

It is their opinion, also, that these tumors arise from the endometrial stroma which they consider to be an undifferentiated müllerian derivative persisting in the adult, and from which various carcinomatous and sarcomatous elements of the tumor may evolve by metaplasia. They point out that in the infant and child and, to a slight extent, in the adult a specific endocervical stroma is present that is similar to endometrial stroma. Occasionally in the infant such a stroma is also seen in the subepithelial layer of the vagina. This would account for the occurrence of mesodermal mixed tumor, such as sarcoma botryoides which is seen in the vagina and cervix of small children, and for the occurrence of mixed mesodermal tumor in the cervix in menstruating women, and in the corpus of the uterus in postmenopausal women. It is problematical whether these tumors arise from displaced embryonal germ tissue, as proposed by Wilms,[11] or whether from rests of heterotopic tissue, which could remain in the endometrium until postmenopausal life and then suddenly produce a rare tumor.

Frequency. These tumors are thought to be very rare but because many are unrecognized or unreported, and because of the confusion in their classification, it may well be that they occur more frequently than is generally supposed. Sternberg and associates, at Charity Hospital, New Orleans, find about the same frequency as leiomyosarcoma of the uterus, and an incidence of 0.08% in patients with gynecological problems. The incidence in various reports appears to be between 1.8% and 5% of uterine malignancies but this probably also includes pure fibrosarcoma and pure leiomyosarcoma.

Parity. There appears to be no difference in incidence between parous and nonparous women.

Location. In early childhood the tumor occurs as a sarcoma botryoides involving the upper vagina or lower cervix and presents itself as a polypoid grape-like mass. During active sex life they arise largely from the cervix and may be similar to a sarcoma botryoides or may be less polypoid. This may depend to a considerable degree upon the duration of the tumor before it is first discovered. In the menopausal and postmenopausal woman the usual site is the body of the uterus. Here also it may be polypoid and cause extensive bleeding. Occasionally in the menopausal woman the tumor may be noted in the cervix; in the premenopausal, it may cause extensive bleeding. Occasionally in the menopausal woman the tumor may be noted in the cervix; in the premenopausal, it may be noted in the corpus of the uterus.

Symptoms. Irregular bleeding, sometimes preceded by serous or purulent vaginal discharge, is the most common presenting symptom. There

may also be pain, abdominal mass, or symptoms relative to the urinary system or bladder.

Prognosis. These tumors are extremely malignant and the prognosis must be guarded. The usual survival after diagnosis is eight to fourteen months.

Treatment. As a general rule these lesions are highly radio-resistant and the only hope for cure is usually considered an early diagnosis and a radical hysterectomy. The lesion extends through both hematogenous and lymphatic channels and tends to spread locally to involve the rectum, lower pelvis, bladder, ureters, and lymph nodes. Distant metastases may be found in the perineum, mesentary, liver, lung, and pleura. Skeletal and brain metastases are rare. It is usually stated that the metastases tend to be either pure sarcoma, pure rhabdomyosarcoma, leiomyosarcoma, or carcinoma—but occasionally mixed metastases have been reported.

SUMMARY

Mixed mesodermal tumors are rare tumors arising from mesodermal stroma of mesenchymatous origin and containing usually 2 or more heterologous elements. They are highly malignant and respond poorly to any treatment. Prognosis is poor but patients, such as the one herein described, occasionally survive longer than the average one year most often reported.

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INCIDENCE OF DEATH among patients with acute myocardial infarction increases with cardiac arrhythmia. The highest mortality is with ventricular tachycardia. For more than 90% of arrhythmias in acute myocardial infarction, digitalis, quinidine, and procainamide hydrochloride (Pronestyl®) are effective. Digitalis is most effective for atrial arrhythmias, probably due to vagal-like action slowing sinoatrial node and delaying atrioventricular node conduction. Normal rhythm may be restored by carotid sinus massage. Treatment of choice for premature beats is quinidine therapy, which also aids conversion of atrial fibrillation after digitalization and is effective for ventricular tachycardia, atrial flutter, and atrial tachycardia. Pronestyl® given orally or administered parenterally with electrocardiographic monitoring is best used in ventricular tachycardia, eliminates premature beats, and may be helpful in atrial tachycardia. Isoproterenol hydrochloride (Isuprel®) is employed in second- and third-degree atrioventricular block. Digitalis therapy is stopped and potassium administered in nodal rhythm. Atrial tachycardia may respond to carotid sinus massage or 1 mg. of neostigmine (Prostigmin®). This drug must be used with caution if the patient has asthma or intestinal obstruction.

MILTON HURWITZ, M.D., and ROBERT S. ELIOT, M.D., Charles T. Miller Hospital, St. Paul, and University of Minnesota, Minneapolis. Arrhythmias in acute myocardial infarction. Dis. Chest 45:616-626, 1964.

Present Trends in Coronary Disease

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ONE-HALF MILLION DEATHS occur yearly from coronary artery disease in the United States. Certain clinical aspects of this problem will be reviewed with emphasis on changing concepts of the last decade. The fundamental knowledge of coronary disease is incomplete, and many controversial issues remain. The opinions expressed are derived from the author's experience and review of the current literature.

ETIOLOGY

An understanding of the causes of coronary disease depends on a knowledge of the pathogenesis of general atherosclerosis and those factors which specifically accelerate the development of atherosclerosis in coronary arteries. The mechanism by which the atherosclerotic coronary artery may be abruptly occluded remains incompletely understood. Epidemiologic studies indicate that multiple factors are involved, including obesity, hypertension, cigarette smoking, diabetes, and elevated serum cholesterol. Each of these factors adds to the risk that overt coronary disease may develop. Emotional factors may precipitate angina pectoris, but their role in causing coronary atherosclerosis or precipitating myocardial infarction is controversial. The evidence incriminating unusual physical stress as an etiologic factor is not convincing.

DIAGNOSTIC CONSIDERATIONS

Angina pectoris. The patient's history is paramount. Classically, substernal pressing pain radiating to the left arm occurs on exertion, but variants in which the distress occurs primarily in the epigastric region, in the neck or jaw, in either arm alone or both arms together, or in the interscapular area are not unusual. The pain sometimes has a burning quality and may be accompanied by eructation, making for confusion with upper gastrointestinal disorders. At times difficult breathing rather than pain may be the patient's complaint. Such patients may indicate that the difficulty is a sense of oppression making it seem hard to get a deep breath. In these cases tachypnea is absent, in contrast to the usual dyspnea of pulmonary disease or left ventricular failure. Precipitation of distress by exertion and prompt relief from rest are important features. Exercise tolerance tends to be decreased in cold weather or on walking into the wind, and also tends to be less in the morning than later in the day. The increased cardiac output which follows a heavy meal or accompanies excitement or anger may cause angina to be present only under those circumstances. Musculoskeletal chest pain at times may be extremely hard to distinguish from angina. Chest wall tenderness is not a feature of angina pectoris. Unfortunately many patients with definite angina have coincidental musculoskeletal reasons for chest wall pain. The response to nitroglycerine may sometimes be the only feature which clearly distinguishes between the 2 types of pain.

The electrocardiogram at rest is normal in approximately 50% of patients with angina pectoris. The majority of patients with normal electrocardiograms will develop ST depressions with a downward slope immediately or two minutes after sufficient exercise. With a classical history, however, the diagnosis has to be regarded as likely even if the exercise electrocardiogram remains normal.

The recording of an electrocardiographic tracing during exertion is now feasible with telemetry, and this too may provide objective verification of the diagnosis of angina pectoris. More extensive experience is necessary before general agreement is reached on diagnostic criteria.

Myocardial infarction. Measurement of serum levels of enzymes released by injured myo-

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cardium represents a significant aid in the diagnosis of acute myocardial infarction. In the presence of left bundle branch block and frequently in the presence of previous infarcts, the electrocardiographic signs of acute infarction will be masked. Additionally, infarcts affecting only the subendocardial two-thirds of the ventricular wall will not affect depolarization (QRS) forces, and determining whether changing T-wave contours in this situation represent frank infarction may be difficult. The normal level of glutamic oxalacetic transaminase (SGO-T) in a given patient varies slightly. Thus, a rise of 10 units or more must be regarded with suspicion even if the peak value does not exceed the so-called normal range. Elevations of lactic dehydrogenase tend to persist longer than elevated SGO-T values. Hence this measurement is of value in patients seen some days after the onset of suspected infarction.

Vectorcardiography has now emerged from the research laboratory and has proved of value in the recognition of electrocardiographically inaccessible infarcts. The vectorcardiogram displays the direction of electrical forces associated with ventricular depolarization from instant to instant in the form of a loop. In myocardial infarction the initial portion of the loop is displaced or distorted by the loss of those forces ordinarily contributed by the infarcted myocardium. The same electrical changes are reflected in the conventional electrocardiograms. However, the electrical axis of the 12 leads ordinarily taken may be such that abnormal Q waves do not develop with infarcts in certain locations. We now recognize that true posterior infarcts result only in widened, taller than normal R waves in V_1. The pattern of anteroseptal infarction when combined with left ventricular hypertrophy may be easier to diagnose by vectorcardiography, as QS complexes in V_1 and V_2 may be seen with left ventricular hypertrophy even in the absence of infarction.

The asymptomatic patient. Silent myocardial infarctions, or those in which symptoms were deemed insignificant by the patient, account for a substantial fraction of all infarcts. The Framingham study demonstrates the value of routine electrocardiograms in this regard. As a practical matter annual cardiograms should be obtained in all male patients beyond the age of 35 and in all postmenopausal women.

Routine exercise electrocardiograms will detect coronary disease in some patients prior to the appearance of symptoms. Practical considerations of expense often influence the selection of patients for such testing, but the test should be utilized particularly in those patients in whom a positive family history, hypertension, and other factors increasing the risk of development of coronary disease are present.

MANAGEMENT OF THE ACUTE PHASE OF MYOCARDIAL INFARCTION

Rest. The patient whose infarct is not complicated by protracted pain, shock, severe congestive failure, or serious arrhythmias may be allowed to feed himself from the start. The effort of using a bedpan often exceeds the cardiac demands involved in the use of a bedside commode with assistance. The cardiac output required for sitting in a comfortable chair is no greater than that in the supine position, and early use of "chair treatment" has become popular. Improved morale and enhanced muscular tone are definite benefits of such a program. In practice, however, it is often difficult to convince the "chair" patient that he should not increase the allowed exertion even further. This constitutes a valid objection to routine use of the more liberal program in the early stages of myocardial infarction. For the patient whose course has been free of any serious complications a three-week period of bed rest often suffices, followed by progressively increasing activities. Patients with very extensive infarcts, or those in whom complications have occurred, may require periods of bed rest of up to six weeks.

Anticoagulation. Thromboembolic complications are decreased with the use of anticoagulants and this has been reflected in decreased mortality rates in many careful objective studies. Patients in whom the use of anticoagulants is most controversial, the so-called "mild coronaries" may become "moderate" or "severe" coronaries subsequent to their initial assessment. The very small risk of complications due to anticoagulant therapy is overbalanced by the risk of delaying anticoagulation in those initially misclassified.

The use of heparin allows anticoagulant effect to be achieved immediately. Other than this advantage for the first twenty-four to forty-eight hours, the prolonged use of heparin alone or combined with coumarin drugs seems to confer no benefit over coumarin drugs alone.

Monitoring. Arrhythmias, particularly ventricular fibrillation, are frequently the cause of death in the first few days following acute infarction. The availability of continuous monitoring equipment combined with an organization of the hospital staff to deal instantly with this emergency will save lives. Such a program should become

routine, probably for a five-day period following infarction.

Fibrinolytic therapy. Prompt dissolution of an occluding thrombus would be desirable, although it is doubtful whether the diagnosis can be made and treatment effected before irreversible changes have occurred in the ischemic myocardium. A decade of investigation in this area has increased our knowledge of this phase of the clotting problem, but adequate laboratory control of the agents used has been very difficult and this approach must be regarded as experimental at this time.

MANAGEMENT OF THE CHRONIC PHASE

Anticoagulants. The desirability of long-term anticoagulant therapy following myocardial infarction has not been established beyond all doubt. However, recurrent coronary thrombosis represents the greatest threat to these patients, and the majority of studies indicate a reduced recurrence rate in patients kept on anticoagulants for prolonged periods. Adequate laboratory facilities for accurate prothrombin time determinations and a high degree of cooperation on the part of the patient are prerequisites if the risk of therapy is to be kept low.

A substantial fraction of patients whose angina suddenly becomes more severe will develop frank myocardial infarcts within a period of weeks. Anticoagulants begun on this indication may prevent a significant number of overt infarcts.

Long-acting coronary vasodilators. No class of therapeutic agents is more difficult to evaluate than these drugs. Angina pectoris is subject to marked spontaneous variation, and considerable benefit often results from placebo effect. The availability of slow-release forms of various long-action nitrites has allowed higher dosages to be administered with fewer side effects and a higher incidence of subjective response. Pentaerythritol tetranitrate (Peritrate®), 80 mg. every 8 to 12 hours, seems as effective as any drug in this class. Patients not helped by Peritrate® occasionally may respond to erythrityl tetranitrate (Cardilate®) or isosorbide dinitrate (Isordil®).

Digitalis and mercurials. The management of congestive heart failure falls beyond the scope of this paper. It is pertinent to note that an exacerbation of angina may be the earliest sign of pulmonary congestion. This should be considered even in the absence of rales, overt edema, or striking chest X-ray changes. If nocturnal cough or unexplained weight gain accompanies increasing angina, a mercurial diuretic may result in dramatic improvement. This may then be maintained with digitalization.

Exercise. Physical activity is both psychologically and physiologically beneficial. Competitive team sports are prohibited as are such strenuous activities as snow shoveling. Lawn mowing, even with power equipment, is often poorly tolerated. Recently, cardiac work evaluation units have been testing indivulals with known coronary disease with work loads simulating such out-of-the-ordinary activities as deer hunting. The fact that a given patient may pass such a test on a given day unfortunately does not prove that he will have no difficulty with similar activity subsequently. The cardiac demands of any task will vary considerably depending on the speed and environmental conditions under which it is performed. These, plus variations in the individual's physiological state at the particular time the task is performed, render such attempts at exact quantitation of a tolerable work load spurious.

Surgery. Internal mammary ligation and talc poudrage have passed their limited vogue. Adequate control series with sham-opreated patients demonstrate that the benefits of these procedures have been derived largely from their potent psychic rather than myocardial effects. Coronary endarterectomy is now technically feasible. The indications for this procedure, or for the coronary arteriography which must necessarily precede it, are still unsettled. Coronary artery disease unfortunately is often multicentric or diffuse, so that an approach which deals with a single overt obstruction will be of value only when the recognized obstruction is indeed the only one, and only when the myocardium supplied by the narrowed vessel has not already been infarcted.

For a while ventricular postinfarction aneurysms were being resected enthusiastically. The natural history of this entity is largely the natural history of the underlying coronary disease, and this should dictate a cautious approach. In an occasional patient with a large ventricular aneurysm, in whom congestive failure is the major problem, and in whom regurgitation of systolic flow into the aneurysm rather than myocardial weakness is the cause of the failure, the procedure may be considered.

PREVENTION

Since our knowledge of the cause of atherosclerosis is incomplete, our advice to the patient concerning its prevention is empirical. High-risk candidates can be identified among patients presenting for routine examinations. Cigarette smoking is associated with a 70% increase in mortality rate from coronary disease, with an even higher

risk for the smoker who exceeds 1 pack daily. An elevated blood cholesterol may increase the risk of developing coronary disease as much as fourfold. Patients with hypercholesterolemia should surely be identified and urged to decrease their animal fat consumption and increase their use of polyunsaturated fats. The use of other therapeutic agents, such as nicotinic acid and thyroid analogues, still requires long-term evaluation. Patients with hypertension die primarily from complications which result from accelerated atherosclerosis. With the advent of better tolerated antihypertensive drugs we are justified in treating benign and relatively mild hypertension. The adverse effect of obesity on life expectancy appears largely reversible with proper weight reduction.

SUMMARY

Fundamental, clinical, and epidemiologic investigations have influenced present concepts of coronary artery disease. The application of such knowledge can be expected to prevent some overt disease, to recognize early disease more readily, and to treat it more effectively.

The author gratefully acknowledges the helpful comments and suggestions of Drs. John F. Briggs and Milton M. Hurwitz in the preparation of this manuscript.

PHEOCHROMOCYTOMAS, if unrecognized, may lead to shock or death after operation for unrelated conditions. The tumors arise from chromaffin tissue, generally within the adrenal medulla but occasionally in extra-adrenal sites. Secondary hypertension results from continuous or intermittent release of catecholamines. The tumors may function paroxysmally. Commonest symptoms are headache, palpitation, and excessive perspiration. Patients frequently have tachycardia, pallor, nervousness, tremor, hyperglycemia, and hypermetabolism. In diagnostic tests, histamine stimulates the tumor to secrete catecholamines and provokes a pressor response, or phentolamine (Regitine®) neutralizes vasopressor effects of circulating catecholamines and reduces blood pressure. Urinary levels of 3-methoxy,4-hydroxymandelic acid, metanephrine, and normetanephrine provide diagnostic clues. The only satisfactory treatment is surgical removal of the tumors, which are malignant in about 15% of cases. Exposure of both adrenals and exploration of the sympathetic chain, para-aortic areas, aortic bifurcation, retroperitoneal area, and abdominal vessels must be done. Intravenous administration of Regitine® may be necessary during the operation to counter dangerous elevation of blood pressure. The need for infusions of levarterenol or blood transfusions should be anticipated after tumor removal, since blood pressure often drops to shock levels. Absence of blood pressure drop may indicate another tumor. Seventy-six patients with pheochromocytomas were studied; 37 had intermittent and 39 continuous tumor function.

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Clinical Aspects of Pulmonary Hypertension

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HYPERTENSION of the lesser circulation differs in many respects from systemic hypertension. First, pulmonary hypertension is almost always secondary to another known factor or disease, in contrast to systemic hypertension which usually represents a primary disease of as yet unknown cause. Furthermore, pulmonary hypertension is not directly assessable by means of clinical examination, since pulmonary artery pressure can only be measured by a rather involved method of cardiac catheterization and is hardly amenable to serial determinations. Finally, pulmonary hypertension is, in proportion, more severe than systemic hypertension; it is seldom significant with elevation of pressure less than twice the normal level, and such high levels as 5 to 10 times normal can still be tolerated by the circulatory system—figures totally unthinkable in terms of systemic hypertension.

As stated, direct determination of pulmonary arterial pressure is not available to the clinician. The diagnosis of pulmonary hypertension, therefore, has to rest upon the consequences of elevation of pressure in the pulmonary artery. Among those are: dilation of the pulmonary vasculature, which may frequently be observed by radiographic examination, right ventricular hypertrophy with or without dilation of that chamber, increased force of closure of the pulmonary valve, occasional regurgitation through this valve, enlargement of the right atrium, and tricuspid regurgitation. Obviously, many of these consequences are related to the severity and duration of pulmonary hypertension, and their presence or absence is variable. Furthermore, clinical signs suggesting the presence of pulmonary hypertension are frequently modified by the disease which caused the elevation of pulmonary arterial pressure.

In discussing clinical diagnostic aspects of pulmonary hypertension one has to consider separately the 3 major component parts of the examination: physical examination, electrocardiography, and radiography.

Physical examination should include a careful examination of the jugular venous pulse. An unusually prominent A wave is frequently found in pulmonary hypertension; large V waves indicative of tricuspid regurgitation may reflect right ventricular dilatation secondary to pulmonary hypertension. Inspection and palpation of the precordium may reveal the presence of a parasternal lift, a reliable sign of significant right ventricular hypertrophy. During auscultation special attention should be paid to the second sound at the upper left sternal border; during inspiration, when the second sound is normally split, accentuation of its later component, which represents pulmonic valve closure, can usually be heard with ease. Occasionally, however, gross accentuation of the pulmonary closure sound may make our ears fail to recognize the split, in which case a single "booming" second sound is heard. When the pulmonary arterial pressure is elevated close to systemic levels the pulmonary valve frequently becomes incompetent from stretching and dilatation of the valve ring. A diastolic murmur of pulmonary insufficiency then becomes audible. This has been recognized for a long time in connection with mitral stenosis as the Graham Steell murmur, but occurs equally often in other forms of severe pulmonary hypertension.

Electrocardiography is probably the most important single diagnostic aid in the recognition of pulmonary hypertension. The electrocardiogram permits with reasonable reliability the diagnosis of right ventricular and right atrial hypertrophy, both of which are the usual consequences of pulmonary hypertension. When these signs are present, the clinician has, however, to consider the fact that other causes of right ventricular and atrial hypertrophy need to be ruled out before the diagnosis of pulmonary hypertension is accepted. Among those are: excessive flow to the lungs, pulmonary stenosis, and tricuspid valve disease.

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The diagnosis of right atrial hypertrophy is made by the presence of tall, narrow, and pointed "gothic" P waves in the conventional extremity leads, usually lead II, and by a prominent positive component of the P wave in right-sided precordial leads. Electrocardiographic diagnosis of right ventricular hypertrophy can manifest itself by 1 of 3 principal patterns: (1) right axis deviation associated with tall R waves in right precordial leads and deep S waves in left precordial leads, (2) right axis deviation, $S_1S_2S_3$ pattern, or left, superior, axis deviation associated with preponderant S waves in all precordial leads, and (3) right bundle branch block. The first pattern is the basic pattern of right ventricular hypertrophy. It is found physiologically in the newborn indicating the normal preponderance of the right ventricle in the fetal and postnatal heart. It is usually found only in severe and long-standing right ventricular hypertrophy, such as congenital heart disease. The second pattern is most characteristically found in patients with chronic cor pulmonale due to emphysema and bronchitis; occasionally it occurs in other forms of right ventricular hypertrophy. Bundle branch block usually signifies right ventricular hypertrophy associated with appreciable dilatation, "diastolic overload," and in congenital heart disease is more often seen in association with large pulmonary flow than with increased pulmonary arterial pressures. Its importance in relation to pulmonary hypertension lies in its occurrence in acute cor pulmonale—sudden pulmonary hypertension leading to dilatation of the right ventricle due to massive pulmonary embolization.

Electrocardiography, valuable as it is in the diagnosis of pulmonary hypertension, has important limitations. Its specificity is high; the fully developed pattern of right ventricular hypertrophy, particularly pattern 1, presents high probability of the presence of anatomic right ventricular hypertrophy. Only rarely can such patterns be confused with a true posterior myocardial infarction and imitated by some unusual forms of right-sided conduction defects. However, the sensitivity of electrocardiographic findings in right ventricular hypertrophy is relatively low, for milder and even moderate degrees of it can be present without any electrocardiographic evidence, or show changes still within the zone of normal variability. For that reason serial records in patients suspected of developing pulmonary hypertension are more valuable and informative in diagnosis than single records.

Radiographic examination may provide important diagnostic clues, particularly in long-standing pulmonary hypertension associated with right ventricular failure. Important radiographic findings include dilatation of the pulmonary artery and enlargement of the right ventricle and right atrium. Dilatation of the pulmonary artery is not specific to pulmonary hypertension. Poststenotic dilatation of the pulmonary artery occurs in association with pulmonary stenosis; that vessel usually is enlarged in conditions associated with large pulmonary flow but with normal pulmonary arterial pressure. Finally, idiopathic dilatation of the pulmonary artery may be confused with pulmonary hypertension. In the presence of dilatation of the pulmonary artery involving its branches the differential diagnosis involves pulmonary hypertension and high pulmonary flow. Chest roentgenogram often provides important clues: In pulmonary hypertension the vascular pattern of the lungs changes abruptly with dilatation involving secondary branches but not smaller vessels. In cases with large pulmonary flow even smallest branches in the periphery of lung fields are filled with blood showing appropriate accentuation of the entire vascular pattern. This differentiation is helpful but occasional errors occur, due to other factors influencing the vascular pattern.

The diagnosis of pulmonary hypertension poses 2 principal problems. First, when a clinician finds definite evidence of pulmonary hypertension, he is obligated to try to determine the cause of it. Second, when dealing with diseases providing potential cause for pulmonary hypertension he should have a high index of suspicion regarding its development. The importance of these 2 points cannot be overemphasized. The diagnostic evaluation of a patient with pulmonary hypertension may lead to discovery of an inapparent yet reversible cause, such as mitral stenosis. Furthermore, alertness in early discovery of pulmonary hypertension may have important prognostic and therapeutic implications.

In fully developed, severe, pulmonary hypertension the clinical diagnosis can be made by using the combined criteria outlined above. However, in many cases the underlying disease obscures or modifies diagnostic criteria to such an extent that the recognition of pulmonary hypertension without cardiac catheterization may be difficult or impossible. Some common diagnostic problems are mentioned below.

Congenital heart disease. In some cases of congenital heart disease pulmonary hypertension is present since birth as an expression of postnatal adaptation and a condition for survival. However, in many patients with major shunting lesions—atrial septal defect, ventricular septal

defect, and patent ductus arteriosus—pulmonary hypertension may develop during varying stages of the disease and may lessen or even eliminate chances of surgical curability. The diagnosis of pulmonary hypertension in such cases may be particularly difficult, because, as already stated, large pulmonary blood flow overloads the right ventricle and produces many similar clinical findings to pulmonary hypertension. Some clinical clues permit a separation of pulmonary hypertension from large pulmonary blood flow with normal pressures but it is usually necessary to perform cardiac catheterization to obtain a definitive answer.

Mitral valve disease, particularly mitral stenosis, produces elevation of pressure in the pulmonary arterial system which is strictly secondary to the high left atrial pressure—passive pulmonary hypertension. This seldom produces clinical signs of pulmonary hypertension since pressure elevation is mild or moderate. However, a significant number of patients develop reactive pulmonary hypertension due to pulmonary arteriolar spasm or disease. The term "pulmonary hypertension" in connection with mitral valve disease usually applies to such cases and signifies a complication rather than a natural sequence of mitral disease. Clinical diagnosis of this secondary pulmonary hypertension is usually easy. Uncomplicated mitral stenosis seldom produces changes in the right side of the circulation to satisfy criteria for pulmonary hypertension. The presence of right ventricular hypertrophy and enlargement and dilatation of the pulmonary artery, and the development of physical signs of pulmonary hypertension almost always point to reactive, secondary pulmonary hypertension. The diagnostic problem posed by mitral valvular disease occasionally concerns cases in which this secondary hypertension in the pulmonary circuit has reached such proportions that it dominates the clinical picture. Some such cases appear clinically to represent primary pulmonary hypertension, and only a careful search reveals the real nature of the disease.

Diseases of the left side of the heart. It is an old pathological observation that the commonest cause of right ventricular hypertrophy is left ventricular failure. As a modernized verision of this relationship one can state that in many patients with chronic left ventricular lesions—hypertensive, ischemic heart diseases, aortic valvular disease, and primary myocardial disease—develop pulmonary hypertension during stages of left ventricular failure, which, in turn, overloads the right ventricle. The mechanism of this is almost identical with that of mitral disease and presents the identical problems concerning diagnosis.

Chronic diseases of the lungs. Chronic pulmonary emphysema, recurrent bronchial infections such as chronic bronchitis, and various forms of pulmonary fibrosis may produce pulmonary hypertension, which is then usually referred to as chronic cor pulmonale. It is now generally believed that chronic hypoxia is the principal factor in the production of pulmonary hypertension. Consequently, it is unusual to find pulmonary hypertension without the presence of cyanosis, polycythemia, and hypercapnia. The picturesque English designation of patients as the "pink puffer" and "blue bloater" aptly presents this point. The first category, which is more common in this country, applies to primary emphysema. Hyperventilation may compensate the respiratory defect and normal blood gases and normal, or insignificantly elevated, pulmonary arterial pressures persist to a terminal stage when rapid deterioration ensues. The second category, more common in England, consists of patients with recurrent bronchial infections with early and variable development of alveolar hypoventilation resulting in cyanosis, polycythemia, and severe enough pulmonary hypertension to cause right ventricular failure with massive edema. In this second group cardiorespiratory insufficiency is often amenable to treatment and, in part at least, reversible.

Clinical diagnosis of pulmonary hypertension in chronic lung diseases may be difficult. Hyperinflated lungs often obliterate clinical and roentgenographic criteria for its recognition. The electrocardiographic pattern, different from the conventional right ventricular hypertrophy, has already been discussed. Its sensitivity is quite low and many cases of significant right ventricular hypertrophy show no diagnostic electrocardiographic changes at all. It is not unusual to miss pulmonary hypertension until frank right ventricular failure becomes apparent.

Primary and embolic pulmonary hypertension. Primary pulmonary hypertension is a rare disease of undetermined etiology. Differentiation of this disease from some forms of congenital heart disease cannot be made without elaborate physiological studies. Furthermore, primary pulmonary hypertension is virtually indistinguishable from its secondary form caused by multiple and repetitive small pulmonary emboli. In such cases clinical recognition of pulmonary hypertension usually presents no major problems since there are no other modifying factors; however, the identification of the nature of the disease usually presents considerable difficulties. A com-

moner form of embolic pulmonary hypertension is its acute form, recognized as acute right ventricular failure from massive pulmonary embolism. The recognition of this disease by the clinician is of great importance as it may be lifesaving by surgical elimination of the sources of emboli, or closure of the pathways of emboli.

SUMMARY

Pulmonary hypertension can be recognized clinically only by its various consequences, mostly its effects upon the right side of the heart. Physical examination, electrocardiography, and roentgenography provide the means for its recognition, and the principal criteria in each of these methods are presented. Since pulmonary hypertension is usually secondary to other diseases, many diagnostic difficulties may arise from the superimposition of primary factors and the secondary pulmonary hypertension.

It is emphasized that the clinician is obligated to investigate the etiology of pulmonary hypertension to the best of his ability. Though not curable, pulmonary hypertension is frequently reversible in response to the elimination or reduction of the initiating factor.

Supported by grant HTS-5498, National Institutes of Health, U.S. Public Health Service.

Presented at the annual meeting, American College of Chest Physicians, San Francisco, June 20, 1964.

BASAL-CELL EPITHELIOMAS of the skin may occur as part of a syndrome, probably hereditary, also characterized by jaw cysts and skeletal defects. The patient often has hundreds of individual skin lesions over the face and trunk. These tumors, which cannot be distinguished histologically from epitheliomas occurring alone, may be recognized and treated early in life but are often considered benign until malignant changes begin to appear at puberty or in adult life.

Cysts occur only in the mandible or maxilla and grossly destroy bone. They may be uni- or multilocular and are similar to other squamous-cell epithelial-lined cysts. Skeletal deformities, usually slight and unnoticed, include bifid or anomalous ribs, mild scoliosis, shortened metacarpals, and frontal bosses. The syndrome may include other deformities of ecto- or mesodermal origin. Treatment is control of the individual lesions. The basal-cell tumors are a problem in long-term management because of their number and tendency to recur. Extensive skin excision and subsequent grafting of the defects may be necessary. With complete enucleation the cysts usually disappear, but recurrences have been reported. Case histories of 2,725 patients with basal-cell epithelioma or epithelioma adenoides cysticum revealed 12 patients with associated cysts and congenital skeletal defects. Similar lesions were reported in relatives of 7 patients.

WALTER D. MADDOX, D.D.S., RICHARD K. WINKELMANN, M.D., EDGAR G. HARRISON, JR., M.D., KENNETH D. DEVINE, M.D., and JOSEPH A. GIBILISCO, D.D.S., Mayo Clinic and Foundation, Rochester, Minn. Multiple nevoid basal cell epitheliomas, jaw cysts, and skeletal defects. J. Amer. med. Ass. 188: 106-111, 1964.

Response of Monilial Vulvovaginitis to Candicidin

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VULVOVAGINITIS CONTINUES to be a common gynecological complaint. Frequently overlooked or disregarded in the past, monilia has been recognized recently to be of major significance as a causative agent. Incidence of monilial vulvovaginitis in clinic populations is reported from 20 to 38%.[1–5] Several reasons have been cited for this increase of moniliasis.

1. Use of antibiotics, especially the broad-spectrum types, may be followed by an acute episode of monilial vulvovaginitis.

2. Increase in known diabetic population due to modern diagnostic procedures identifies a particular disease group that is highly susceptible to moniliasis. The diabetic with this infection is difficult to cure.

3. Predisposition of the pregnant patient to monilial irritations is well documented.

Candida (monilia) albicans is the common etiological agent and is easily and accurately identified by using Nickerson's medium. Common symptoms of the disease are pruritis, dysuria, and discharge. The clinical findings are quite typical in most cases, but O'Brien[1] reports clinical error of up to 60% when clinical impression is compared with culture results. Therapy with previous methods has left much to be desired.

An antifungal antibiotic, candicidin (Candeptin®), was reported by Lechevalier[6] to be particularly active against yeast, especially C. albicans. Candeptin® is chemically related to nystatin but was found to be 100 times as potent as the latter on C albicians, in vitro.[7]

MATERIAL AND METHODS

A 1 gm. vaginal tablet containing 3 mg. of Candeptin® was prepared for clinical use and made available for this study.

Inclusion of patients in this study was restricted to those who (1) had complained of vulvovaginitis, (2) had clinical symptoms of this disorder, (3) had a positive culture diagnosis of moniliasis using Nickerson's medium, (4) had followed the therapeutic regimen outlined to them, and (5) had returned for follow-up examination and culture.

Forty-four patients comprised the series. Five were treated for infection episodes which occurred six weeks or more after being symptom-free and culture-negative. Thus, 49 case episodes have been included. Three of the recurring infection episodes followed antibiotic therapy. One case was a diabetic patient with early diabetic acidosis and glycosuria.

Patients were instructed to insert one Candeptin® vaginal tablet high in the vagina twice daily, using a vaginal inserter provided. Fourteen days of therapy were prescribed. Douching and intercourse were restricted, the latter to guard against reinfection. With one exception (Case BLC 11,290 listed below) no other medication was administered during the treatment interval.

On completion of the fourteen-day therapy, patients were instructed to discontinue the preparation and return for examination and vaginal culture. If the culture showed persistent monilial growth, a second course of treatment was instituted. Patients with negative cultures were requested to return three days later for another culture. No douching or intravaginal medication was permitted in the interim. A further confirmatory culture was taken four weeks later.

Patients were considered cured only when symptom-free, when the clinical examination confirmed the absence of vulvovaginitis, and when the culture was negative. They were questioned about possible side effects. Time of symptom relief after therapy began was noted. Patients were instructed to interrupt therapy immediately if unpleasant reactions occurred. The vagina in these patients was carefully inspected with a speculum.

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TABLE

EFFECT OF CANDEPTIN® VAGINAL TABLETS ON MONILIASIS IN GRAVID AND NONGRAVID PATIENTS

	Gravid	*Nongravid*	*Total*
No. of patients in first course of treatment	30	19	49
Cures after first course of treatment	27 (90%)	18 (95%)	45 (92%)
Cures after second course of treatment	30 (100%)	19 (100%)	49 (100%)

RESULTS

Of the 49 cases, 4 required a second course of therapy. This is a primary cure rate of 92%. After fourteen days of further medication, all 4 were symptom-free and had negative cultures, thus producing a 100% cure (see table).

There were no systemic or local side reactions. Most patients experienced symptomatic relief in twenty-four to forty-eight hours after therapy was started. Twenty-one were pregnant, 2 in early postpartum period. All gave birth to normal, healthy infants.

Symptoms in 7 of the cases, 13.7%, followed the use of antibiotics, usually with acute onset of severe symptoms. One of these cases was so severe it warrants a brief comment.

Case BLC, No. 11,290. A 29-year-old multigravida, nonpregnant patient who had previously been treated with broad-spectrum antibiotics, was unable to sit, walk, or submit to pelvic examination. She was hospitalized for severe ulcerative vulvovaginitis. Heavy monilial cultures were obtained from vulvar and vaginal areas. She was treated with Candeptin® tablets intravaginally, twice daily, light cradle, and moist Burrow's packs. Initially, she required narcotics for pain and pruritis. Rapid recovery allowed discharge of the patient in a few days, and culture was negative at that time. Topical corticosteroids were also used to lessen ulceration and induration externally. She was cured at the end of two weeks' therapy. Culture remained negative.

COMMENT

Candeptin® has been demonstrated to be a potent agent against C. albicans. It acts locally. In the concentration used in the vaginal tablet for this study there was no untoward reaction or side effect.

The medication and treatment regimen received good patient acceptance in this group. This was especially true if the patient had been previously treated unsuccessfully. Since symptom relief was relatively rapid in most cases, the author had to stress need for completion of a full fourteen-day course of therapy.

Use of other agents for treatment of moniliasis has been disappointing to many investigators. Nystatin locally has been reported to be from 52 to 89% effective.[8–10] Gentian violet and its derivative products cause a great deal of patient objection and do not always provide any patient relief. Staining of clothing and the added office visits required are logical reasons for complaint.

Others have reported excellent results using some form of Candeptin®. Abruzzi[11] reported a larger series with 82% cure from a first course of therapy and 90% after a second course. Giorlando[12] reported exceptional results using Candeptin® prepared as an ointment. In a series of 154 patients, he recorded a cure rate of 100% in those receiving the therapeutic dose and treatment regimen comparable to the tablets.

In our study Candeptin® gave rapid and lasting symptomatic relief. Retreatment for two additional weeks was required in only 12% of the patients, following which all but 2 were cured. The remaining 2 patients failed to appear for a follow-up culture after the second course of treatment but reported they were symptom-free. Although a small and selected series, it suggests that Candeptin® is a highly effective drug, specific for moniliasis, and with no adverse reaction.

SUMMARY

A specific antimonilial agent, Candeptin®, gave excellent results with 1 fourteen-day course of therapy, 92%. Retreatment gave an overall cure rate of 100%.

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Pulmonary Tuberculosis

Current Concepts

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THE TUBERCULOSIS DEATH RATE has greatly decreased. The tuberculosis case rate has fallen more slowly, and even less so in metropolitan areas. However, New York City has had increasing tuberculosis morbidity rates for the past two years and Los Angeles County for the past year. Tuberculosis is a large subject and only the aspects of X-ray case finding, pathogenesis, and therapy will be discussed here.

CASE FINDING

Several examples of routine chest films taken when a patient sought medical care for some nonpulmonary ailment are presented to emphasize the value of this procedure for all patients seeking medical attention. Sputum studies for tuberculosis were secured because of the abnormal film, although these patients had no respiratory complaints.

CASE REPORTS

Case 1. CJF, 57 years old, sought medical attention because of malaise. The routine chest roentgenogram was abnormal (Fig. 1). Concentrates and cultures were heavily positive for tubercle bacilli.

Case 2. EJG, 67 years old, came to the hospital because of intermittent constipation. The routine chest roentgenogram revealed right apical infiltration (Fig. 2). Three gastric cultures were positive for tubercle bacilli.

Case 3. BEJ, 41 years old, had pain in his left shoulder. Tuberculosis and diabetes mellitus were both diagnosed for the first time because of routine chest X-ray (Fig. 3) and urine studies. Three sputum cultures were positive for tubercle bacilli.

Case 4. CL, 35 years old, noticed a lump in his throat. Chest roentgenogram revealed bilateral disease, but especially involving the left lung (Fig. 4). Sputum concentrates and cultures were heavily positive for tubercle bacilli.

With the knowledge that more than 50,000 Americans develop active tuberculosis each year, and that 30,000,000 are tuberculin positive, indicating that they have been infected, it is clear that tuberculosis is worthy of discussion.

PATHOGENESIS

The primary focus can be found in the lung in most cases of tuberculous infection. As organisms reach the draining lymph nodes, these, together, are called the primary complex. Animal studies have revealed that a few tubercle bacilli leave the draining hilar lymph nodes and enter the main thoracic duct and the bloodstream with lymphohematogenous seeding within hours of the primary infection, which is the secondary stage. These organisms may reach the pleura, prostate, bone, kidney, or meninges. In most cases the organisms are walled off and there is no further difficulty. In some patients, twenty to thirty years after primary infection, tubercle bacilli in an organ such as kidney or bone may multiply to produce active disease. This is the tertiary stage of tuberculosis, corresponding to the tertiary stage of syphilis, where there is active disease in extrapulmonary sites years after the primary infection.

In most cases the primary tuberculous infection is easily controlled and there may simply be a residual calcified primary focus or primary complex. In some children, however, the primary infection is not controlled and progresses to active pulmonary tuberculosis.

Reinfection adult type tuberculosis is usually seen a number of years after the primary infection and is related to the breakdown of caseous foci. If this material liquefies and excavates, a cavity results. Bacilli may spread by direct ex-

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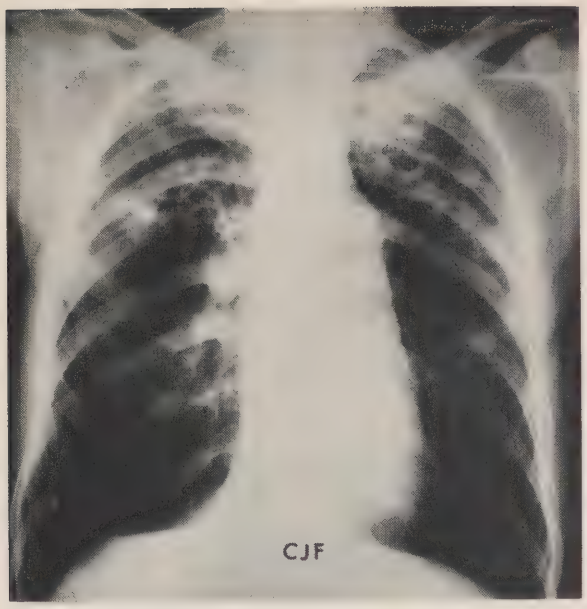


Fig. 1. Case 1

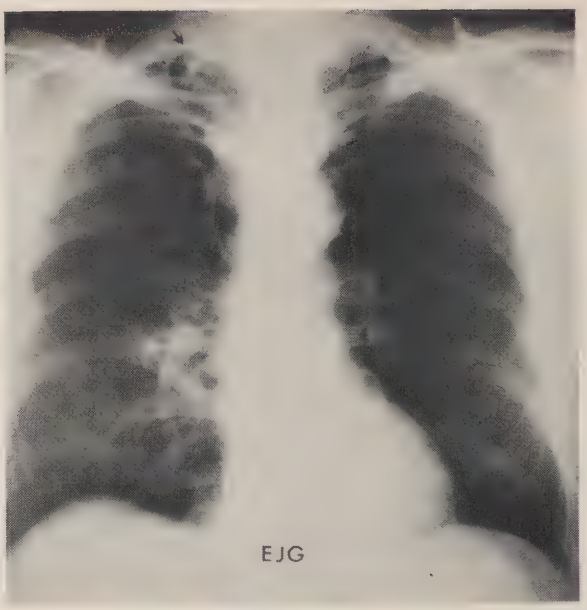


Fig. 2. Case 2

tension or by bronchi, lymphatics, or bloodstream.

Healing is related to the death of bacilli, closure of cavity, and resolution of bronchopneumonic exudative disease and fibrosis.

CLINICAL OBSERVATION

Minimal disease is apt to be asymptomatic and is detected by skin test in children or chest X-ray in the adult. An asymptomatic patient may have a positive tuberculin skin test and the chest X-ray may reveal a small bronchopneumonic patch of tuberculosis. If the disease is untreated it will usually progress and enlarge. Ultimately the patient may note cough, sputum, low-grade fever, or general malaise. Other symptoms that may appear are blood streaking and weight loss. Chest pain may be noted with pleural involvement.

The chest X-ray is an integral part of the physical examination, and will usually reveal disease before the appearance of physical signs or symptoms. Naturally, the earlier the diagnosis of tuberculosis is made and therapy instituted, the less lung tissue will be destroyed.

Since tuberculosis must be considered in the differential diagnosis of most pulmonary abnormalities, skin tests and sputum studies for tuberculosis and fungi should be instituted early. It is well to remember that some patients may have 2 pulmonary diseases simultaneously, as tuberculosis and coccidioidomycosis or tuberculosis

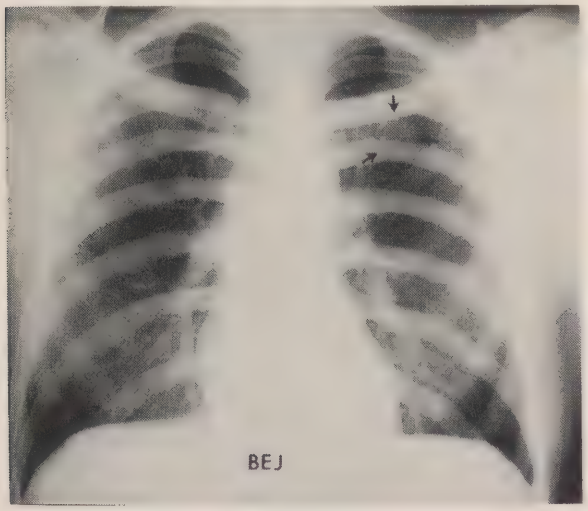


Fig. 3. Case 3



Fig. 4. Case 4

TABLE 1

DOSAGE OF SOME TUBERCULOSIS DRUGS IN ADULTS

Drug	*Route*	*Usual dosage*
Isoniazid	Oral	300 mg. daily
Streptomycin	Intramuscularly	1 gm., 2 times a week (often given daily for first month)
Aminosalicylic acid	Oral	4 gm., 3 times daily
Ethionamide	Oral	250 mg., 3 to 4 times daily
Cycloserine	Oral	250 mg., 3 to 4 times daily
Pyrazinamide®	Oral	500 mg., 3 times daily

and bronchogenic carcinoma. Serial chest films are important as well as the securing of previous chest films to compare with present X-rays.

THERAPY

To suppress microbial activity and halt the progress of the disease and destruction of lung tissue as quickly as possible, antituberculosis chemotherapy using isoniazid (INH) with para-aminosalicylic acid (PAS) or streptomycin is instituted (Tables 1-4). Choice and dosage of drugs may vary somewhat. Before starting drug therapy, sputum or gastric washings should be secured for cultures and antibiotic susceptibility determinations, but one should not await these results because they will not be reported until four to eight weeks later.

The basic principles of tuberculosis antibiotic therapy are: (1) concomitant administration of two drugs, usually, and including INH, especially in cavitary disease, (2) continuous administration of these drugs, and (3) prolonged administration of these drugs to insure healing and to prevent relapse.

A good standard basic regimen is INH 300 mg. and PAS 12 gm. daily, orally. Numerous studies have revealed no advantage in using higher doses of INH, or using steroids, except possibly in semicomatose patients. A third drug is usually not required[1] as results are not superior and toxicity is greater with 3 drugs (Fig. 5, Tables 5 and 6). If the patient is acutely ill or toxic or has multiple cavities, most physicians will, however, add 1 gm. of streptomycin, intramuscularly daily, for thirty to forty-two days to the basic regimen of INH and PAS. Patients with persistent positive sputum after five to six months of antituberculosis drug therapy, especially if cavity persists, should be evaluated for possible surgical resection of the major disease area and addition of other tuberculostatic drugs or both. About 2 to 4% of our admissions with active pulmonary tuberculosis require resectional surgery, usually lobectomy.

INH alone can be used for posthospital drug

TABLE 2

ISONIAZID (INH)

Chemistry	isonicotinic acid hydrazide
Absorption	readily from gastrointestinal tract
Distribution	widely throughout body fluids
Excretion	predominantly by kidneys
Toxicity	peripheral neuritis is rarely observed with standard dosage. Pyridoxine is effective therapy for neuritis, but is not necessary for routine use.

TABLE 3

PARA-AMINOSALICYLIC ACID (PAS)

Chemistry	PAS
Absorption	easily absorbed from gastrointestinal tract but varies with type of preparation
Distribution	in body fluids and tissues
Excretion	rapidly and mainly in urine; variable smaller amounts in feces
Toxicity	mainly gastrointestinal intolerance, especially common in patients with peptic ulcer or previous gastric surgery

TABLE 4

STREPTOMYCIN (SM)

Chemistry	composed of streptidine, streptose, and glucosamine
Absorption	very poor from gastrointestinal tract. Rapid after intramuscular injection; peak in about one hour
Distribution	in extracellular fluids; only small amounts in pleural fluid and normal cerebrospinal fluid
Excretion	60 to 90% in urine
Toxicity	mainly impairment of vestibular function; about 2 to 5% of patients receiving 1 gm., twice weekly, and more than 10% with larger doses. Toxicity is more likely after total doses of 60 to 90 gm.

TABLE 5

ROENTGENOGRAPHIC CHANGE AFTER THERAPY WITH THREE ("TRIPLE") AND TWO ("DOUBLE") DRUG THERAPY IN MULTIPLE CAVITARY TUBERCULOSIS
(modified from Small[1])

	SM + INH + PAS	*INH + PAS*
Total number treated	235	263
Comparison of six-month X-ray with pretreatment X-ray		
Number patients reviewed	192	211
Marked improvement	36%	36%
Moderate improvement	38%	36%
Slight improvement	21%	21%
No change	4%	6%
Worse	1%	1%

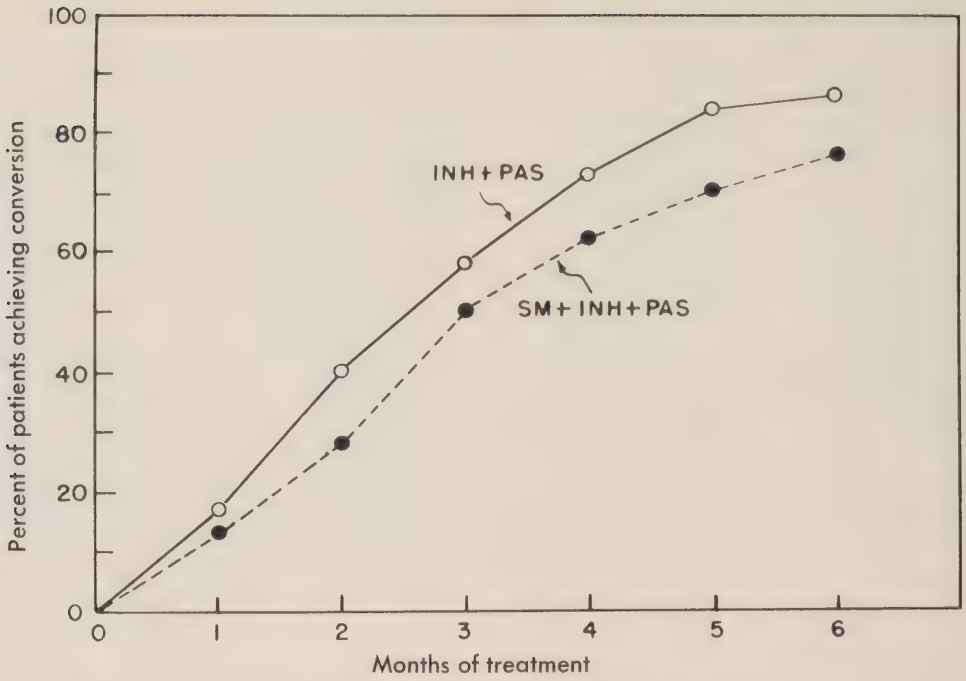


Fig. 5. Comparison of sputum conversion in patients receiving 2-drug and 3-drug regimens as initial therapy (from Small[1])

therapy for the patient with inactive tuberculosis, in treatment of primary tuberculosis in children or recent tuberculin conversion in an adult, and for patients with a positive PPD skin test who are receiving corticosteroid therapy for some other illness. For all practical purposes, INH alone is equally effective as INH-PAS in non-cavitary, minimal, or moderately advanced disease (Fig. 6). It is our policy to treat with INH alone all patients with abnormal chest X-rays compatible with granulomatous disease and a positive tuberculin skin test, despite negative sputum studies for tuberculosis, since a significant number of such patients already have or will develop active tuberculosis (Table 7).

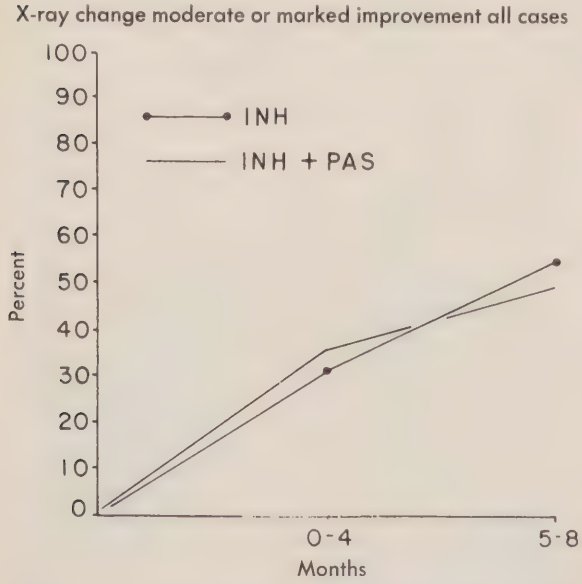


Fig. 6. Comparison of sputum conversion in patients with minimal or moderately advanced noncavitary tuberculosis receiving either INH alone or INH-PAS as initial therapy (from Phillips[2])

Patients with active tuberculosis are best treated in a hospital and followed with 1 or 2 sputum cultures each month. Chest X-rays are secured monthly for the first few months and thereafter bimonthly. Planigrams of the disease area are usually secured at the onset of therapy and periodically thereafter to determine the status of any cavities visualized.

Depending on the extent of disease, the patient's age, or presence of other infirmity, patients with pulmonary tuberculosis are usually fully ambulated after two to six months of continuous sputum culture negativity and stable chest films. Almost all patients can return to their former occupations provided they continue on INH after discharge from the hospital. There is very little need for rehabilitation or vocational guidance for tuberculosis patients in this modern chemotherapeutic era.

All patients who have had pulmonary tuberculosis should be followed with semiannual sputum studies and chest X-rays for the rest of their lives. With tuberculosis drug therapy, relapse

TABLE 6

DRUG TOXICITY AFTER TRIPLE AND DOUBLE THERAPY
(modified from Small[1])

Drugs causing toxic reaction	*Number of patients having drug stopped*
SM + INH + PAS Group (235 patients)	
SM	25
SM + INH	2
SM + PAS	4
SM + INH + PAS	1
INH + PAS	1
INH	3
PAS	19
Total	55
INH + PAS Group (263 patients)	
INH	7
PAS	25
INH + PAS	1
Total	33

TABLE 7

RATES OF DEVELOPMENT OF CLINICAL TUBERCULOSIS
(data from Murray[3])

1. Negative tuberculin skin test	0.9 per 1,000
2. Negative chest film and positive PPD	3.2 per 1,000
3. Abnormal chest film and positive PPD	25.2 per 1,000

rates are low—about 1 to 2%, but constant vigilance is necessary to control and eradicate tuberculosis.

SUMMARY

Taking routine chest films at the hospital or physician's office is a valuable tuberculosis case detection procedure.

Therapy should be instituted promptly. An excellent basic regimen is 300 mg. of INH and 12 gm. of PAS daily. INH alone should be continued for two to four years after the last positive sputum, depending on the extent of disease.

Patients with a chest film compatible with granulomatous disease and a positive tuberculin skin test should receive INH for twenty-four months.

With prolonged INH therapy, relapse rates are only 1 to 2%.

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INTERVERTEBRAL DISK INFECTIONS may cause abdominal pain that sometimes results in exploratory laparotomy before the true source of the pain is discovered. Spinal neoplasm, inflammation, trauma, and spondylolisthesis have previously been reported to cause pain referred to the abdomen if the eighth thoracic through the first lumbar nerve roots that supply the abdominal wall are involved.

The most frequent symptom of disk infection is an almost constant backache that is accentuated by activity; spasmodic pain in the lower abdominal quadrants often may mask the back pain and lead to a suspicion of intra-abdominal disease, or radiation into the testicles may suggest genitourinary disease. Roentgenogram of the spinal column, however, shows narrowing of an intervertebral disk, erosion of vertebral end plates, and new bone formation bridging the disk space. Erythrocyte sedimentation rate is elevated, but leukocytosis and fever do not always accompany disk infections.

Complete immobilization of the spinal column usually leads to spontaneous fusion of the affected segments; other treatment is seldom required. Antibiotics may delay spontaneous fusion and should be given only when systemic signs indicate infection spread.

C. ROGER SULLIVAN, M.D., and RICHARD E. SYMMONDS, M.D., Mayo Clinic and Foundation, Rochester, Minn. Disk infections and abdominal pain. J. Amer. med. Ass. 188:655-658, 1964.

The Psychiatry of Presidential Assassination

Part IV: Truman and Kennedy

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PRESIDENT HARRY S. TRUMAN AND OSCAR COLLAZO AND GRISELIO TORRESOLA, NOVEMBER 1, 1950

Of the eight armed attacks on American Presidents, the only one that probably was an organized conspiracy was the assault on the guards at Blair House by Oscar Collazo and Griselio Torresola, who were attempting to reach and kill President Harry S. Truman. The two gunmen were members of the fanatical Puerto Rican Nationalist party, which advocated complete independence of Puerto Rico. At his trial, Collazo testified that he had hoped the assassination of the President would cause a revolution that would enable Puerto Rico to break away from the United States.

Puerto Ricans by birth, Collazo and Torresola were 36 and 25 years old, respectively, at the time of the assassination attempt. On the afternoon of October 31, 1950, they took the mid-afternoon train from New York City to Washington, a city neither had visited before. With prudent economy they bought one-way tickets; neither expected to return to New York and neither did. Arriving in the capital that evening, they registered under assumed names at a hotel near the railroad station and began making their plans with the aid of a city map.

The next morning, November 1, they took a cab to the vicinity of Blair House, across Pennsylvania Avenue from the White House. Blair House, for many years a residence for visiting dignitaries, was the temporary home of President Truman while the White House underwent extensive repairs. Only a narrow yard, a low hedge, and, part way along the front, an iron picket fence separated Blair House from the sidewalk, on which pedestrian traffic was heavy. Passing by the house in the cab, the two gunmen noted the positions of the guard booths on the sidewalk at the east and the west ends of the building. After their reconnaissance, they had lunch and returned to the hotel. Torresola, who had a thorough knowledge of firearms, taught Collazo, who did not, how to load and dry fire a Walther P-38 automatic pistol. After almost two hours of practice, they oiled their pistols (Torresola had a Luger), filled the clips, put extra cartridges in their pockets, and set out again for Blair House.

President Truman had been busy all morning in his office in the White House. At 1 P.M. he rode to Blair House for lunch. After eating, he went upstairs to take a nap. The afternoon was hot, and the President stretched out on top of his bed.

While the President slept inside, Collazo and Torresola walked past the entrance to Blair House to further study the layout, paused at a distance, and decided on their tactics. Separating, they approached Blair House from opposite directions along Pennsylvania Avenue, planning to meet at the steps of the house. In the guard booth on the west, the side from which Torresola approached, sat Leslie Coffelt, a White House policeman. In the east booth, toward which Collazo walked, Joseph Davidson of the White House police was talking to Secret Service Agent Floyd Boring. Standing under a canopy over the front steps of Blair House was Donald Birdzell, another White House policeman.

Unnoticed among the pedestrians on the sidewalk, Collazo reached and stopped at a position about 8 ft. from Birdzell's back. He drew his pistol from his trousers, took aim, and pulled the trigger. Misfiring, the gun produced only a loud click. As Birdzell turned, Collazo began hitting the pistol with his fist. The weapon fired, sending a bullet into Birdzell's right leg. In spite of the wound, the policeman ran to the middle of the street to draw Collazo's fire, turned, and began shooting at the gunman, who was just starting up the steps. From the east guard booth Davidson and Boring opened fire on Collazo but could not hit him squarely because the iron fence stop-

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ped or deflected their bullets. Another Secret Service agent, stepping from a door at the east end of Blair House, fired one shot at the gunman. Collazo soon fell to the sidewalk with a bullet in his chest. Meanwhile, an agent on duty inside Blair House had armed himself with a Thompson submachine gun and stood ready to cut down anyone reaching the top of the outside steps.

At the time of Collazo's abortive attempt to shoot Birdzell in the back, Torresola had reached the other guard booth, Luger in hand. Standing at the doorway, he fired three shots at Coffelt, causing him to collapse. Torresola quickly turned on another White House policeman, who had just been entering Blair House by a basement door when the shooting began, and felled him with three bullets. After jumping the front hedge to reach Collazo on the steps, Torresola fired at Birdzell in the street, hitting him in the left knee. Coffelt, although near death, leaned from his booth, took careful aim at Torresola, and put a bullet into his head. Torresola fell dead behind the hedge and the battle was over. Twenty-seven shots had been fired in less than three minutes. Awakened by the shooting, President Truman went to the front window and saw Collazo sprawled on the sidewalk. A guard noticed him and yelled at him to get back.

Collazo was taken to a hospital, where physicians found that his wound was not serious. Charged with murder and assault, he was brought to trial on February 27, 1951.

He believed, he testified at his trial, that the United States had illegally seized Puerto Rico as an act of imperialist aggression during the war with Spain in 1898. He contended that Spain already had granted Puerto Rico an autonomous status and that, therefore, the Treaty of Paris, in which Spain ceded the island to the United States, was invalid.

He shouted from the witness stand that for the preceding fifty years Puerto Rico had been exploited by American capitalism and that island home rule was merely a façade behind which the United States wielded all essential political power.[1]

These and similar views were shared by the 500 or so members of the Nationalist movement in the United States. Some government officials believed, but could not prove, that Collazo and Torresola were part of a larger conspiracy to kill the President that was directed by Pedro Albizu Campos, president of the Nationalist party.

The attorneys appointed to defend Collazo considered entering a plea of insanity. Collazo bitterly opposed such a plea, however, feeling that it would make a mockery of the cause in which he believed so deeply and for which he was willing to sacrifice his life. Dr. John R. Cavanagh, a competent and well-known psychiatrist, examined him twice and concluded that he was not mentally ill.

Collazo was found guilty and sentenced to death. A week before the date set for the execution, President Truman commuted the sentence to life imprisonment. Oscar Collazo is in a federal penitentiary.

PRESIDENT JOHN F. KENNEDY AND LEE HARVEY OSWALD, NOVEMBER 22, 1963

The personality of Lee Harvey Oswald seems to be familiar if one is acquainted with the previous assassins. For Oswald, too, was mentally ill when he shot President John F. Kennedy, Governor John B. Connally, Jr., and policeman J. D. Tippit that autumn afternoon in 1963. On the basis of newspaper and magazine accounts of Oswald's life, there is not, in my opinion, any reasonable doubt that the assassin had paranoid schizophrenia. Indeed, a tentative diagnosis of incipient schizophrenia had been made years before by a New York psychiatrist.

Oswald is the only assassin to deny that he had harmed anybody, even though witnesses saw him shoot Officer Tippit. All the other assassins confessed with alacrity, even with pride. Several testified to their deeds with the awe of a man convinced he had been instructed personally by God. It is possible that Oswald still clung to the hope that by silence and denial he might be freed and be allowed to go to Russia, this time as a person of importance who would receive a hero's welcome. In all likelihood, there will never be any way of knowing what the delusions in Oswald's mind were that impelled him to try to kill former Maj. Gen. Edwin A. Walker in April 1963 and, later in the same year, to murder a man whose political views were the opposite of the general's. What the two men had in common at the time Oswald shot at them was their high rank (and hence their high status as figures of authority).

All the assassins and would-be assassins, including Torresola and Collazo, seem to have had a malicious hatred of authority together with a compelling need to strike back to obtain their idea of justice. This phenomenon is readily apparent in Zangara, who was taken from school by his father and put to a man's work when he was only 6 years old. Hatred of a powerful father before whom a boy is helpless can become a murderous loathing later on, the father now symbolized by figures of authority in general. To kill the greatest and most powerful figure of authority in the world must, to such a wounded mind, contain not only the seeds

of destruction but also immense inner gratifications. That there is fame of a sort in killing a President cannot be denied. Although quest for fame through assassination would little more than bemuse the person of sound mind, such a motive is difficult to dismiss entirely. With the exception of John Wilkes Booth, all the assassins were little people, unknown except when their failures had momentarily attracted the attention of others. Had they not killed a President, or tried to, they would be nonentities. However, that the desire for fame is the chief motivation for seeking to assassinate a President, an idea sometimes put forward, is difficult to uphold. Public revenge against an assassin is too swift and certain to permit a sane person to seriously consider the act. Mental illness, with its hallucinations, delusions, and faulty perception of reality, is the key ingredient in Presidential assassination in America. Even the deed of Torresola and Collazo, who probably were not mentally ill, looks like an insane act, because a rational man born and reared in the United States cannot understand how the murder of the President would have aided the cause of Puerto Rico. Rather, he would see the act as a deep stain on Puerto Rico's honor and hence as a disadvantage to her. Perhaps Torresola and Collazo, coming from another culture, saw it differently.

Lee Harvey Oswald, her third son, was born to Mrs. Marguerite C. Oswald on October 18, 1939, in New Orleans. His father, Robert E. Lee Oswald, had died of a heart attack two months before the boy's birth. Mrs. Oswald had little money with which to support her three children. For the first two years of Lee's life she was able to stay home with him. Later she went to work, and at age 3 Lee was placed in a boarding school for children who had lost at least one of their parents. His older brothers were already at the school.

In 1944 Lee's mother met an industrial engineer from Boston; they were married the following year—the third marriage for her—and moved to Fort Worth, Texas. Mrs. Oswald brought Lee back into the home with her; his older brothers were sent to a military academy in Mississippi. The marriage lasted only three years. In his divorce action against Mrs. Oswald, her husband complained that she nagged him, argued about money, once had thrown a bottle at him, and another time had scratched him. For the next four years Lee (aged 9 through 13) lived with his divorced mother in a small frame house in Fort Worth.

After the assassination, reporters of *Life* magazine[12] interviewed many persons whose lives had brushed Lee Oswald's life in some way. Families in the block remember that Lee was quick to take offense. One man said, "He seemed antisocial to me. I thought he was vicious with other children. He would become quite angry at very little provocation." Lee's first teacher in elementary school, with whom he became fairly close, said, "Lee left an empty home in the morning, went home to an empty home for lunch, and returned to an empty home at night." His grades deteriorated as he advanced from grade to grade, perhaps because of his emotional turmoil. His I.Q. was 103.

"Lee finished the sixth grade at Ridglea West [Elementary School] in June 1952. He was approaching his 13th birthday—fairly tall for his age, well built and athletic. But he appeared lonely and wore an increasingly noticeable chip on his shoulder. At this time his mother decided to go to New York, a move that was to have a great impact on Lee. She said she wanted to be close to her son John Pic, by her first marriage, who was stationed in New York with the Coast Guard."[12]

Lee's emotional difficulties, up to now mostly covert, came out into the open. His grades in junior high school were barely passing, and he was frequently truant. On his report card he was rated unsatisfactory in cooperation, dependability, and self-control. His truancy brought him to the attention of school authorities and the New York Children's Court. The probation officer of the court found that Mrs. Oswald had no appreciation of her son's psychological problems or her relation to them. He recommended that Lee be committed to a children's psychiatric facility, but the boy returned to school. Mrs. Oswald refused to take him to a psychiatric clinic.

At about this time Lee was examined by Dr. Renatus Hartogs, chief psychiatrist at New York's Youth House for Boys, at the request of the Bronx Children's Court. *Life* summarized his report after the assassination:

> It was apparent that Oswald was an emotionally disturbed, mentally constricted youngster who tended to isolate himself from contacts with others, was suspicious and defiant in his attitude toward authority, and overly sensitive and vengeful in his relationships with his peers. He saw himself as being singled out for rejection and frustration, Dr. Hartogs said, but did not seem to have developed the courage to act upon his hostility in an aggressive or destructive fashion. He also appeared to be preoccupied about his sexual identity and his future role as a male.
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> He was guarded, secluded and suspicious in his dealings with the psychiatrist. He had to be reassured that information he gave would not be used against him, but to help him. He could not become verbally productive

and talk freely about himself and his feelings. About his mother he would state only that she was "O.K." He had ambivalent feelings about his mother—a strong need for maternal warmth but also an awareness that only a limited amount of affection was available. He protected himself against disappointment by not reaching out to others.

Dr. Hartogs concluded that here was definitely a child who had given up hope of making himself understood by anyone about his needs and expectations. In an environment where affection was withheld, he was unable to relate with anyone because he had not learned the techniques and skills which would have permitted it. A diagnosis of incipient schizophrenia was made, based on the boy's detachment from the world and pathological changes in his value systems. His outlook on life had strongly paranoid overtones. The immediate and long-range consequence of these features, in addition to his inability to verbalize hostility, led to an additional diagnosis: "potential dangerousness."

Dr. Hartogs' report was sent to Children's Court with the recommendation that the child be committed to an institution for his own protection and that of the community at large. He felt that treatment might have led to improvement, and that ultimately the boy would have been rehabilitated. His recommendation was not followed.

(The psychiatrist said he was not surprised when Lee Oswald was arrested for the assassination of President Kennedy. "Psychologically," he said, "he had all the qualifications of being a potential assassin. Such a criminal is usually a person with paranoid ideas of grandiosity who can get satisfactory self-vindication only by shocking the entire world and not just a few people. He had to show the world he was not unknown, that he was someone with whom the world had to reckon. When he was 13 he reacted negatively, by withdrawing. It took him a whole lifetime to develop his courage, and then all the accumulated hate and resentment came out. A person like Oswald resents a lifetime of being pushed to the sidelines. He culminates his career of injustice-collecting by committing a supreme, catastrophic act of violence and power.")[12]

In 1954 Lee and his mother returned to New Orleans, and Lee entered the eighth grade. A former classmate interviewed by *Life* recalled, "He fought with a lot of guys. I don't remember him friends with anyone." Many ex-schoolmates used the word "loner" to describe him. He graduated from junior high school in 1955. That fall, he entered high school, but in less than a month he had dropped out, his mother having written the school that they were moving to San Diego. Actually, they remained in New Orleans for ten more months, Lee staying out of school and spending much of his time reading in the library. He tried to enlist in the Marine Corps after his 16th birthday, in October 1955, but was turned down because of his youth.

In August 1956 Lee and his mother moved back to Fort Worth, and he entered a high school there. A grade school acquaintance noticed a striking change in him: "He looked like he was just lost. He was very different from the way I remembered him. He seemed to have no personality at all. He couldn't express himself well. He just hadn't turned into somebody. He hadn't turned into anybody. I've read where people say he was a loner. Well, he wasn't in the sixth grade but he sure was in high school."

In October of 1956, just after turning 17, Lee dropped out of school again and joined the Marine Corps. In conversations with *Life* reporters,[12] former associates and superiors of his in the service recalled that he was different. A fellow trainee at boot camp said: "He was pretty hard to understand. I remember him as quiet, serious and trying to find himself. The rest of us used to wrestle and horse around, but he would have his bunk in the corner and stay there, reading a book. He didn't have any friends." His section chief at Camp Pendleton remarked: "He was good with a rifle, but he was such a hothead I was glad when he was finally shipped out for radar training. He was always having beefs with the guys."

In July 1957 Oswald was sent to Atsugi Naval Air Station, Japan, where he was to be a radio technician for fifteen months. A former barracksmate at Atsugi said about him: "He was a real oddball. He used to bring up this stuff about his name, Lee. He was proud of it because he said he was named after Robert E. Lee. He thought Robert E. Lee was the greatest man in history. He used to get in lots of fights, but he didn't make out too well. He had a temper, but wasn't too good a fighter." Another former member of Oswald's outfit said: "I remember him as being very quiet, but wild when he was drunk. . . . But he was mostly by himself, and never showed up at any of the squadron parties."

Twice in 1958 Oswald was court-martialed, once for not registering a pistol he owned and once for challenging a noncommissioned officer to fight. He was reduced in rank from private first class to private.

In October 1958, his foreign duty completed, Oswald was reassigned to a Marine base near Santa Ana, Calif. Here he began to study Russian by himself, his plans for the future apparently set by now. His commanding officer recalled: "He read most of the time—histories, magazines, books on government and a Russian newspaper he used to get. . . . There were no pocketbooks or comics for him." The C.O. also remembered that Oswald baited officers: "He would ask officers to explain some obscure situation in foreign affairs, just to show off his superior knowledge. He seemed to be in revolt against any kind of authority." For a brief period Oswald was an end on the squadron football team, but

he was thrown off the squad for talking back in the huddle.

In the summer of 1959 Oswald's mother wrote her son that she had been injured in an accident at work and had used up her savings to pay medical bills. Granted a hardship discharge, Oswald returned home, ostensibly to care for her. But he remained only three days; soon he was in New Orleans, awaiting departure of a boat to Europe. By mid-October 1959 he was in Russia. Not long after his arrival in Moscow, he went to the U.S. Embassy, turned in his passport, and declared that he had applied for Soviet citizenship.

When his defection became known in Moscow, two Americans interviewed him. One of them was Aline Mosby, a correspondent for United Press International.

> The interview gave [Oswald] an opportunity, for the first time in his life, to feel important. His opinion was sought. His picture was taken. He responded by being as articulate as he had ever been in his life. He struck Miss Mosby as "a person very determined but unsure of himself, naive and emotionally unbalanced."
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> "I am a Marxist," Lee told her. "I became interested at about the age of 15. I've seen poor niggers, being a southern boy, and that was a lesson. People hate because they're told to hate, like school kids. It's the fashion to hate people in the United States."[12]

The other interviewer, Priscilla Johnson, then a correspondent for North American Newspaper Alliance, later recalled:

> Among the feelings Oswald could not conceal . . . was anger, directed mainly, at the time, against officials of the U. S. Embassy in Moscow. These officials, Oswald felt, had stalled him when he tried to take an oath renouncing his American citizenship. Here the tension between his feelings and his effort to suppress them became articulate: "I can't be too hard on them. But they are acting in an illegal way."
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> . . . . . .
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> "My mother has been a worker all her life," he went on, "having to produce profit for capitalists. She's a good example of what happens to workers in the United States." . . . I asked whether his mother was disillusioned, like him, or worn-out beyond her years? "That's the usual end of people in the United States, isn't it? . . . It's the end of everyone, in any country. It's a question of why they end up that way. For whom and under what system they work." . . .
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> Since Oswald had traveled thousands of miles to build a new life in Russia, I expected that he would be wasting no time learning all he could about the country. He would be anxious, I assumed, to see how the socialist economic theories he believed in were working out in practice. That was where I had my biggest surprise. The life he was leading in Moscow was a dismally lonely one. Most of each day he spent sitting alone in his hotel room waiting for the telephone to ring. If he thought it was his mother calling from Fort Worth to beg him to come home, he wouldn't answer. Every time it rang, though, he hoped it was some Soviet official calling to announce that his request for citizenship had been granted.
>
> . . . He insisted that he had seen the "whole city of Moscow" and "the usual tourist attractions." But he would not name a single landmark he had actually visited. For all his struggle to get to Moscow and his efforts to stay, he appeared to lack even the curiosity of the ordinary American tourist.
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> . . . Not only was he not looking at the life all around him. He was making an heroic effort not to see it.
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> . . . . . .
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> That Oswald did, in fact, see himself as extraordinary came out unexpectedly when I asked him why he had been willing to grant me an interview at all. I expected a simple response. That he was homesick, maybe, and wanted someone to talk to. Instead, he surprised me. "I would like," he replied, "to give the people of the United States something to think about."[13]

Although the Russians refused to grant Oswald citizenship, probably because they judged him to be a crackpot,[14] after a long delay they gave him permission to stay in their country as a resident alien. (In his diary,[15] Oswald said that after being told, a few days after his arrival in Russia, that his visa had expired and that he would have to leave the country, he slashed his left wrist in a suicide attempt. He was kept in a hospital for a week, part of the time in a psychiatric ward, he wrote. In September 1964, however, his wife threw doubt on the validity of the diary, saying that he wrote it later to make an impression on the American people.)

The Soviet authorities sent Oswald to Minsk, giving him a job in a radio factory as a metalworker at about $90 a month. Soon he began to complain about the unappetizing food, the crowded living quarters, and the political pressure exerted on civilians. He joined a rifle club, he later claimed, and became an expert rifleman. The Marine Corps, in the meantime, gave Oswald, still a reservist, an undesirable discharge because of his attempt to renounce his U.S. citizenship. In a letter of protest to John Connally, who Oswald thought was still Secretary of the Navy but who had recently resigned, he said: "I shall employ all means to right this gross mistake or injustice. . . ."[16]

In the spring of 1961 Oswald met Marina Nikolaevna Prusakova, a pretty 19-year-old pharmacist from Leningrad. Although he was unpopular, she married him, in part, apparently, because she felt sorry for him. "Everybody hated him," she said later, "even in Russia." He had begun, before he met Marina, to negotiate with the U.S. Embassy in Moscow in the hope of returning to the United States. Sixteen months later, he departed for America with his Russian wife and their recently born daughter. The State Department, deciding that Oswald was still an

American citizen, had loaned him $435.71 with which to come home.

After arriving in Fort Worth in the summer of 1962, Oswald and his family lived briefly with his brother Robert and then with his mother before moving into an apartment of their own. He had serious difficulty getting a job because he had defected to Russia and because his wife was Russian. Finally he obtained one in a welding shop as a sheet metal worker. Although his work was satisfactory and his attendance record perfect, he quit suddenly in early October and went to Dallas. There he found work as a trainee in a photographic firm, rented a small apartment, and sent for his family. Two incidents later reported to *Life* interviewers[12] took place about this time: Marina left her husband for a while after he had beaten her for smoking, and she had her daughter baptized in secret because Oswald, an atheist, was opposed to the ceremony.

In March 1963 Oswald, using the name "A. Hidell," ordered an Italian carbine from a sporting goods company in Chicago. By this time Marina was pregnant again. Early in April Lee lost his job as a photo printer because, officials of the firm later claimed, he was incompetent.

On April 10 Oswald hurried out of the apartment after supper. At about 10:30 Marina discovered a note, written in Russian, telling her what to do should he disappear or be imprisoned. Arriving home late that night, Oswald told his wife that he had shot at former Maj. Gen. Edwin A. Walker, an advocate of right-wing causes. The bullet, after crashing through a window, had just missed Walker's head. Oswald explained to Marina that Walker deserved to be killed because he was fascist. She kept the note and said she would use it against him if he repeated such an act.

Toward the end of April 1963 Oswald went to his birthplace, New Orleans, to look for work. He got a job, beginning on May 10, as an oiler of coffee processing machines and rented a cheap apartment for himself and his family. According to his landlady, he was unpleasant and inconsiderate. Twice he erected pro-Castro signs on the front porch without asking her permission. On July 19 he was fired from the job at the coffee company for unsatisfactory work. During 1963 his mental health apparently deteriorated to such an extent that he could not concentrate consistently and therefore became incompetent in his work.

While in New Orleans, Oswald organized his own Fair Play for Cuba Committee, of which he was the only member. He distributed handbills and other material on the streets. Once, he was arrested after a dispute with three anti-Castro Cubans.

Late in September Oswald went to Mexico City and applied at the Cuban and Russian embassies for a visa that would permit him to return to Russia by way of Cuba. Told that an answer to his request might take three months, he became angry and left for Dallas, near which Marina and their daughter were now living with a friend. He rented a room of his own downtown under an alias and agreed to visit his family on weekends. Through the woman with whom his wife was staying, Oswald obtained a job at the Texas School Book Depository. A few days later Marina gave birth to their second child, another girl. On at least two weekends in November, Oswald was seen firing a rifle at a range near Dallas. A customer at the range was impressed by the excellence of Oswald's shooting.

On November 19 the Dallas newspapers announced the route that President Kennedy's motorcade was to take through the city on the 22nd. (The procession was part of a two-day combined political and nonpolitical trip to Texas that the President had planned several months beforehand.) On the route of the motorcade was the Texas School Book Depository, which the President's car was scheduled to pass at about 12:25 P.M., during Oswald's lunch period.

On the evening before the day of the assassination, Oswald showed up unexpectedly at the house where Marina and the children were staying, ate dinner, played with his daughters, and went to bed early. He left the house early the next morning without waking Marina and walked half a block to the house of a fellow employee with whom he was to ride to work. On the back seat of the car he placed a long package made of wrapping paper. The package contained curtain rods, Oswald told his co-worker. The worker noted that Oswald took the package with him when they entered the school book warehouse.

Oswald apparently put in an ordinary morning of work. At noon an employee on the sixth floor invited him to go down to the street with him to watch the motorcade; Oswald told him to go ahead without him. A half hour later, just after the Presidential car had passed by the front entrance of the depository, a shot rang out; two others followed in quick succession. A motorcyle policeman in the caravan looked up and saw startled pigeons flying from the top of the depository. He sped to the building, parked his motorcycle nearby, and shoved his way through a group of spectators. At the entrance he encountered the building superintendent, who had come outside to watch the procession. Together

they entered the building and ran to the elevators at the rear. Since neither of the two elevators was on the first floor, the two men dashed up the stairs nearby. From the second floor landing the policeman noticed a man in the lunchroom and, gun in hand, rushed in upon him. The superintendent identified the man as Lee Harvey Oswald, an employee, and the two men continued their climb to the top of the building.

About one minute later the clerical supervisor of the company saw Oswald walking through the offices on the second floor toward stairs that would take him to the main entrance. At about 12:40 he got on a bus at a point seven blocks from the depository. The driver reported later that Oswald told him, "The President has been shot," and then laughed.[16] The bus was making little progress in the traffic jam caused by the motorcade and the assassination. Oswald got off and a few minutes later entered a taxi. He arrived at his rooming house at about 1 P.M. Now in a real hurry, he soon ran back out, zipping up a jacket.

About fifteen minutes later at a point not quite a mile from Oswald's rooming house, Patrolman J. D. Tippit of the Dallas police stopped his patrol car and called to a man on the sidewalk who had the general appearance, now being broadcast by police radio, of the suspect described by a witness to the assassination. The man came over to the right side of the vehicle. Tippit got out on the left and started to walk around in front of the car. The suspect, Lee Oswald, drew a revolver and quickly fired several shots. Four hit Tippit, killing him instantly.

As he walked rapidly from the scene, Oswald discarded the cartridge cases and, in a parking lot, his jacket. Hearing a police siren, he stepped quickly into the entranceway of a shoe store. The manager saw him, noticed that he was out of breath and frightened, and watched as he entered a nearby movie theater without buying a ticket. Notified by the shoe store manager, the cashier of the theater called the police. The theater was soon surrounded, and the house lights were turned on. Several policemen approached Oswald, sitting in a back row, after the store manager pointed him out. Oswald struck one of them with one hand while drawing his revolver with the other. The policeman grabbed Oswald's gun and, with the help of his fellow officers, subdued him. Handcuffed, Oswald was driven to police headquarters, arriving at about 2 P.M.

On the morning of November 24 Oswald was to be transferred from the city jail to the county jail. Flanked by detectives, he stepped from the basement office of the jail into the glare of spotlights. As the nation watched on television, Jack Ruby, a nightclub manager and owner, slipped through a surging crowd of newsmen and detectives, pointed a .38-caliber revolver at Oswald's abdomen, and fired a single, fatal shot.

During hours of intensive questioning, Oswald had vehemently denied shooting either President Kennedy or Officer Tippit. He had refused to take a lie detector test.*

SUMMARY

Since the birth of this country, eight attempts have been made to assassinate Presidents. Four were successful. With one exception, none of the murders, actual or attempted, was the result of foreign or domestic intrigue. Rather, each was the product of one man's disordered mind. The exception, the attempt by Collazo and Torresola in 1950 to shoot their way into Blair House and kill President Truman, was the result of a conspiracy by a few Puerto Ricans, the purpose of which, as they saw it, was to help Puerto Rico. They had no thought of overthrowing the United States government.

Except for the two Puerto Rican gunmen, then, who probably were not insane (after the battle only one was alive to be examined psychiatrically), the assassins, in my opinion, had schizophrenia, in most instances a paranoid type. The causes of this disease are not known. Parental rejection, broken homes, lack of a strong male figure with whom a boy can identify, and emotional stresses severe enough to prevent the developing child from dealing successfully with his fellowmen are often associated with paranoid schizophrenia. Repressed homosexual drives have been assumed to be psychological constituents in paranoid illnesses, but the relationship is not known to be certain.

Lawrence's family was intact, although very little is known about the personalities of his parents or the conditions that existed in his home. Booth's father, psychotic in episodes, was away much of the time, and the growing John Wilkes saw little of him; he died when the boy was 14. Guiteau's father probably was mentally ill, and his mother died when he was 7. Czolgosz came from a poverty-stricken background, and his mother died when he was 12. Schrank was only

*My account of the assassination was written before the *Report of the President's Commission on the Assassination of John F. Kennedy* (Warren Report) was released to the public. The Report does not state that a psychiatrist examined Oswald anytime during the two days that he lived after the assassination, hence it is safe to assume that he was not examined by one. Although the Warren Report contains a wealth of detailed information, no new data of psychiatric importance are brought to light, in my opinion.

7 when he lost his father through death; his mother soon abandoned him to an uncle and aunt. Zangara came from an intact family but missed the common experiences of childhood, forever resenting the fact that his father had put him to work when he was only 6.

Oswald, whose father died just before his birth, never had a significant male figure to imitate. His mother, who was eccentric, who tended to reject him, and who understood little or nothing of his problems and her contributions to them, laid the seeds of hatred of authority which were to grow to psychotic proportions. Of great importance in understanding Oswald's displaced resentment may be the fact that Marina, his wife, apparently used his sexual inadequacy as a weapon in the frequent arguments they had. If his desires were predominantly homosexual (repressed), such jibes, by threatening his masculine defenses, could not have failed to produce enormous angers. It is possible, although we shall never know unless new facts come to light, that the shootings in April and November of 1963 were psychotic attempts by Oswald to prove his toughness and aggressiveness (that is, his masculinity) to Marina and to the whole world, to which he could not adjust.

The ease with which four Presidents were killed and four others were attacked clearly shows that trying to lock up all firearms, ammunition, and psychotic persons motivated by one reason or another to kill a President is unfeasible. If the distressing history of Presidential assassination is to end with John F. Kennedy, adequate protection of the President is essential. Very likely, more Presidential cooperation than has been apparent in the past will be required. Also, the American people must acquire a new understanding of why their President cannot mingle freely with them. Because international tensions and constant teetering on the brink of nuclear war seem to be the order of the day and because an attempt to assassinate the Commander in Chief of the U.S. Armed Forces might well be a preliminary to war (to create confusion that would blunt American retaliation), the position of the President with respect to his security appears to be quite different from what it once was. The nuclear age has imposed the need for a change in political behavior. The President who follows the old practices and traditions of mixing freely with the people and shaking their hands would appear to stand convicted of reckless behavior toward the country of which he is head.

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IN TESTS FOR PANCREATITIS, a conservative upper normal limit of urinary excretion of amylase is 300 Roe units per hour. This level was selected after determining amylase excretion in a two-hour collection of urine from 100 persons without pancreatic, gastrointestinal, or renal disease. Statistical analysis of the data showed a mean value of 127 Roe units per hour and a standard deviation of 64. The upper level of 300 was selected to minimize danger of a low figure, which would falsely indicate pancreatitis, or, conversely, a high value which would fail to indicate true pancreatitis.

EARL E. GAMBILL, M.D., and HAROLD L. MASON, PH.D., Mayo Clinic and Foundation, Rochester, Minn. J. Lab. clin. Med. 63:173-176, 1964.



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J. ARTHUR MYERS, M.D.
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DURING the first thirty-seven years of the University of Minnesota School of Medicine, no single person played a greater role in its development than Dr. Richard Olding Beard. He was born in Middlesex, England, in 1856, came to the United States at the age of 13, and grew up in Chicago. When he was 26 years old, in 1882, he received the degree of Doctor of Medicine from Northwestern University and moved to Minneapolis to engage in practice. A year or so later, while attending a medical meeting where a clinical problem was presented, Dr. Beard entered the discussion from the physiological point of view. The next day he was offered a professorship of physiology on the faculty of the Minnesota Hospital College. The following day a similar invitation came from the faculty of the St. Paul Medical School. He accepted the first offer.

Many years later, in 1921, he said: "I should like to paint for you the picture of the old Winslow house, on Main Street Hill upon the site of the old exposition building . . . where the Minneapolis college had a lecture room or so and some 20 beds and wherein the present speaker began the teaching of physiology with nobody and nothing to help him but what he had in his head and could get to the tip of a somewhat awkward tongue. . . . I could tell you many enlivening stories of those early days, and among them, of the midnight ride of Paul Shillock, now Colonel in the U.S. Army, and a group of his student associates; conveyance, a hired horse and wagon; arms, a few shovels; destination, Lakewood Cemetery; objective, a newly made grave; capture, a rare prize in those days, a 'stiff'; surprise, by unexpected enemy, a sheriff's posse; get-away by the boys, barring Colonel Shillock, who, missing the tail-board of the rapidly disappearing wagon, fell a prisoner into the arms of the sheriff and was bailed out next morning by a deeply shocked and duly astonished faculty. And the interesting sequel to that story is that the stiff, not having any friends, was dissected before all that was left of him was returned to his empty grave!"

Concerning the first class he taught, Dr. Beard counted it among the honors of his service as a medical educator that Dr. Arthur J. Gillette of St. Paul and Dr. George G. Eitel of Minneapolis were his students. Dr. Beard was a strong advocate of the union of Minnesota Hospital College with the newly authorized University College of Medicine and Surgery. When this school and the St. Paul Medical School united with the University College in 1888, he was appointed professor of physiology and thus became a member of the original faculty of 29 members of the College of Medicine and Surgery at the University of Minnesota. He attended the first meeting of this faculty on June 8, 1888.

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Soon after its organization, Dr. Beard was elected secretary of the faculty. This kept him in close contact with the other original members as well as all new appointees. His position also necessitated that he be in close touch with Dr. Perry Millard, who was the first dean of the college. Dr. Beard contributed greatly to development of the curriculum and other necessary work preparatory to opening the college for the first class of students on Oct. 1, 1888. There was no available building on the university campus to house the New College of Medicine and Surgery. Therefore, the offer of the building of the Minnesota Hospital College, located at Sixth Street and Ninth Avenue South, Minneapolis, was accepted. In this building all teaching of laboratory subjects and some lectures on clinical subjects were conducted. The hospitals of the Twin Cities, both public and private, provided facilities for clinical teaching. The course covered three years of six months each. The fees were $35 per annum. Dissecting material was extra and scarce.

In 1893 the college was moved to a new building known as Medical Hall on the university campus. Concerning this Dr. Beard wrote: "It was the occasion of great concern when the Medical College was removed. The Academics were practically the entire University of that day, and the invasion of the Campus by the Medics was like the alarum of the barbarians at the gates of Rome. They were literally afraid of us and, perhaps, not altogether without occasion, for the Medics of the period, hard-working, ambitious, critical as ever, were a rough lot. To 'pass up' a student over the amphitheater benches was a common pastime, and if discovered by the entry of a professor, they were not in the least abashed; to conceal animals, large or small, dead or alive, in the reading-desk or under the seats; to mix the chemical solutions so that the reactions would not work, to introduce a 'stiff' into a faculty meeting—these were quite ordinary pranks. If a lecture was liked, it was always applauded. Silence greeted the unappreciated, and those who were in disfavor might meet empty benches or be treated to a small riot."

From the beginning of the University College of Medicine and Surgery, Dr. Beard served as secretary of the faculty or administrative board, with the exception of a few years, throughout his faculty career. He became assistant dean in 1913. Thus, with each new dean, Dr. Beard was the source of information concerning the school's evolution. He had been present when every link of the chain of progress was welded and indeed he himself forged a considerable number of links.

Dr. Beard's interest in the school was so abiding, he was so meticulous in all of his work, and he had such a command of the English language as to be most convincing, that he was a forceful leader.

Throughout the first thirty-seven years of University of Minnesota School of Medicine, Dr. Beard participated in every administrative activity. His attendance at executive faculty and later administrative board meetings was unequaled. In fact, his absence due to illness on May 29, 1908, was the first since the school was established. He worked diligently to elevate the standards of medical education. In the beginning the medical course covered a period of six months per year, for three years. When he retired in 1925, the course required six years of nine months each and an additional year of internship.

It was Dr. Beard who played the leading role in departmentalizing the College of Medicine and Surgery in 1909. It was he who was responsible for establishment of the University School of Nursing in 1909, promoting it even after his retirement. It was he who initiated appointment of a committee to study and make recommendations pertaining to sanitary conditions on the campus, including protection of the health of students in 1910. He had an important part in President Vincent's reorganization of faculty and establishment of an affiliation with the Mayo Clinic program.

Concerning the reorganization of the medical school he, in 1921, wrote: "In 1912, the so-called 'reorganization of the Medical School' was undertaken. Its announced purpose was to diminish the size of the Faculty. It involved the retirement of men who had given long and valuable service to the University and had served, in many instances, without salary. It included readjustments of position of undoubted merit in certain cases. That its primary stated purpose was a mistaken one is shown by the fact that within three years the original numbers of the faculty had been regained by new appointments, and that at the present time the Faculty is larger than it was before the reorganization was effected.

"No constructive effort,—and I have no doubt of the constructive intention which inspired that effort,—ever worked for any school the dire destruction of fraternal feeling, of successful autonomy, of team-playing cooperation which this event involved. Slowly and painfully the School has passed through the succeeding years of convalescence toward the hope of recovery, and it is still convalescent."

Six years after establishment of the Mayo Clinic affiliation he wrote: "In October, 1914, a

committee was appointed by the Administrative Board to consider the possible relationship of the Mayo Clinic to the Medical School. Objections arising to an affiliation with the Mayo Clinic, the Doctors William J. and Charles H. Mayo established the Mayo Foundation for the Promotion of Medical Education and Research with an endowment which has now reached the sum of nearly two million dollars. After a long and disquieting controversy, resolutions were finally adopted by the Faculty in March, 1915, which approved an affiliation between the Medical School and the Mayo Foundation. By action of the Board of Regents the affiliation was effected, but with the Graduate School, instead of the Medical School. Some two years later, this temporary affiliation was replaced by a permanent union with the immediate transfer to the University of the endowment fund for the support of the Foundation.

"The gift was a generous, nay, a princely one. The foundation is, in itself, a magnificent conception. Its potentialities for good in the service of the public and in the promotion of medical education are unmeasured. But it remains a matter for the keenest regret that by reason of influence we cannot analyze, nor even comprehend, this great good should have been secured at so sad a sacrifice of some of the best teaching ability in the Faculty and at the cost of so much of the good-will of the Alumni and of the profession of the state."

When one lists and studies every forward step of the school between 1888 and 1925, Dr. Beard's participation is in evidence. One of his last outstanding efforts was the chairmanship of the committee on endowment for the schools of medicine and nursing. He proposed this activity on Nov. 6, 1923, and his committee was appointed on Nov. 22. On Dec. 6, the committee recommended that the administrative board organize the endowment plan and that a joint committee be appointed to conduct a campaign for endowment funds. This was accomplished, and the committee proceeded under Dr. Beard's chairmanship with well-known success. Mrs. F. C. Todd, Mrs. Gale, and Mrs. Mapes presented the university with $45,000. This was supplemented by $110,000 of university funds and enabled the university to build an eye, ear, nose, and throat hospital. The Citizens Aid Society, at the instance of Mrs. George Chase Christian, gave $250,000 for the building and equipment of the cancer institute. Mr. William Henry Eustis gave in money and in property the amount of $1,500,000 for a children's hospital, a children's convalescent home, and their endowment. In 1925, President Coffman said, "If this movement continues there is no reason why we should not have built here at the University of Minnesota as great a Medical Center as can be found anywhere in the world."

Dr. Beard had such a command of the English language that he was in demand both as a speaker and writer. When Dean Millard died in 1897, President Northrup made a special request of Dr. Beard to prepare the memorial. Dr. Beard later said, "I demurred for there had been occasions of conflict between this militant Dean of the early days and his equally militant secretary." Nevertheless, he prepared a beautiful memorial. Some years later President Northrup said to Dr. Beard, "There is something I want you to do for me. If I should go on into the other world before you do and should there be an occasion to write a memorial for me, I want you to write it." The opportunity came, and thus another of Dr. Beard's classical memorials appeared. During the years he was on the faculty he wrote a memorial for every member who died. Concerning this he said "The performance of that duty has been the more possible because of my intimate knowledge of the character and the sterling service of the men with whom I have worked; but nevertheless in the doing of it I have often thought that we might better have written the memorial, better have spoken the words of it, put them into print, that the recipient might have read them before he had passed on."

President Vincent's reorganization of the school of medicine and his promotion of the affiliation with the Mayo Clinic caused much enmity among physicians who lost faculty positions and those who strongly opposed the affiliation. After President Vincent resigned, minor attacks were still directed at Dean Lyon and Dr. Beard, inasmuch as Dr. Beard had supported President Vincent in the reorganization of the faculty, and he and Dean Lyon gave support to the affiliation with the Mayo Cilinic.

Concerning this he said, in 1925, "I cannot look into a large future for the Medical School in which the medical profession of the State does not play its part. There are few of us but deplore any past occasion of difference with its members. The School needs their cordial support. It hardly seems just that differences of judgement upon past events should alienate their interest or deny to the School their encouragement and help. I plead with you all that for your part and through your influence with your professional associates you seek to level the barriers which any such differences have raised. Let us ask the profession to forget dissension and to abate criticism; to get

together and to think together and to think greatly in behalf of the School."

The unpardonable sin of originating and disseminating false rumors to defame his character was committed. Rumors even circulated among the students. As always, many persons who heard such rumors accepted them without attempting to determine their authenticity.

> "Who steals my purse steals trash;
> Tis something, nothing;
> Twas mine, tis his, and has been slave to thousands;
> But he who filches from me my good name,
> Robs me of that which not enriches him,
> And makes me poor indeed."
>
> WILLIAM SHAKESPEARE
>
> (Iago speaking, Othello, Act 3, Scene 3, pp. 157.)

Fortunately those who had worked most intimately with him and many others promptly recognized the falseness of circulating rumors. On June 12, 1925, before he was to retire on July 1, members of the board of regents, the faculty of the school of medicine, and a group of friends gave a testimonial dinner for him at the Minneapolis Club, with President Coffman presiding. President Coffman closed his introductory remarks with, "All in all, he has been a great influence; a leader who emphasized fundamentals and saw far into the future."

Mr. Frederic B. Snyder, president of the board of regents said, "While you have done many things in the upbuilding of the Medical School of the University of Minnesota destined to carry your name forward when you are gone, it is safe to predict that the task you have undertaken, since your retirement, to raise an endowment for the Medical School, will bear fruit not only in gifts while you are active, but long afterwards when wills and testaments are opened and reveal bequests and legacies which without your efforts woud never have been made."

In speaking for the administrative board, Dean Lyon said: "In an institution some men are very intimately and fundamentally related to its destiny. Such a man in this Medical School has been Dr. Beard. He has been a part of its brain, a part of its coordinating and planning mechanism, a part of the institutional consciousness. When such a man leaves it is like taking out a brain center. The loss can never be fully replaced." Dean Lyon also said: "It is a great honor to Dr. Beard that he is one of the founders of this Medical School, which has accomplished so much and which appears to have such a large and useful future. Its high standards, its capable facilities, its excellent reputation, its large outlook and its plans for expansion are largely the work of his hands and his brain." In reviewing the twelve years he had worked with Dr. Beard, Dean Lyon said: "I can truthfully say that not one accomplishment, not one advance, not one plan of these 12 years but has been largely influenced, shaped and invigorated by Dr. Beard."

Dr. Orville M. Meland, president of the medical school alumni said: "One can hardly think of the Medical School without recalling its teachers. Of these teachers one stands out prominently; not only because of his winning personality, but because of his untiring efforts in building up the School to what it is today. After two or more hours in the laboratory . . . Dr. Beard lectured to us. He was always prompt. Stepping in briskly, he delivered a finished, polished discourse on some physiologic subject, and then as promptly disappeared. Here was laid the foundation for our clinical medicine. Those days have changed . . . . To us he has not changed. He is a little bit older, a little grayer, but his eye is still keen. To us he is the same Dr. Beard.

"Dr. Beard I wish to extend to you the congratulations, the love and the appreciation of the alumni. We wish you God-Speed."

Speaking for the faculty, Dr. S. Marx White, who became a member in 1898, said: "The Medical School of the University of Minnesota has been distinguished as being manned by a group with high ideals and great desires for the advancement of medical education. In all these years there has been no movement with which I have been personally acquainted which has not borne the impress of Dr. Beard's hand. He has had an active, effective and directing influence in all the advanced movements that have been made and they are many."

Marion L. Vannier, director of the school of nursing said: "Probably no other man is so well known to the Nursing Profession. His articles and public addresses on the subject of Nursing Education have been read and appreciated by thousands of Nurses in this country and abroad. In other words, Dr. Beard is an international figure in the nursing world and it is largely through his influence that the University of Minnesota School of Nursing has become so well and favorably known."

Speaking on behalf of the committee of arrangements of the evening, J. C. Litzenberg made a presentation in appreciation of Dr. Beard's long years of service: "This is an appreciation written by loving hearts and I may add that it was made by an artist with loving hands. When I asked the Medical School Art Shop to do this, the Head asked that she might do it herself because of her long association with you and her admiration of you and your work." Miss Jean Hirsch was the artist.

When Dr. Beard was told of the testimonial dinner to be given on June 12, 1925, it was suggested that in his response he devote his time to reminiscences. However, he demurred. He said, "The past is of value only so far as it is funded into the present, . . . into the character of the men who have made the present what it is." When he was introduced by President Coffman he made no reference to his thirty-seven years of progressive work in the development of the school. He said, "I should not have declined the invitation to talk reminiscences to you tonight. I should not have taken up this forward-looking task if I had not had vision to see and faith to believe that this Medical School of ours has a large future." He then proceeded to point out important needs for further development of the school much of which might be provided by the committee on endowment.

He presented his vision of the future of the school of medicine as follows: "With a natural union of the naturally allied forces of the faculty, alumni and professions, there need be no limit to the natural growth of the School, to the spread of its influence, to the realization of the values it may render to the public 'whose we are and whom we serve.'

"With the faith and the affection I hold and have held in the Medical School, from its beginning to the present day, I can see a large vision of its future and the future of medical education in Minnesota for which we have long hoped and waited, a vision that has sustained us through years of difficulty and doubt and disappointment and sustains us yet. A born optimist, I love to look into the horoscope of its future and find there something to work for still.

"I see a School of sufficient capacity, its laboratories adequately manned and equipped, its clinical material abundant to its teaching needs, opening wide its doors to every properly prepared and fitly selected student who would enter. I would tenaciously cling in such a school to the principle of intelligent selection of the human material which may fitly be educated by the State to serve the State in preventive and remedial medicine.

"I see an equipment of hospital services, suitably endowed for the investigation of the causes of disease and the methods of their prevention, for the application of modern science upon the ever advancing crest of its progress to the diagnosis, the treatment and cure of disease. I see this hospital of the future the most effective mechanism for the restoration of the sick to health and to economic efficiency.

"I see a medical library and a medical literature in the Minnesota school, complete and accessible, that will contribute its quota of funded influence to the education of graduate and undergraduate students alike; that will invite the use by the profession of a circulating system; that will serve to extend the knowledge of the people at large in the things that belong unto their health. I see the time when the University will take up the task of sending suitable information to the public, in the interest of the public health and in substitutions of the miserable husks of knowledge fed to it by the lay and the pseudo-medical press.

"I see the Minnesota School making its large perennial contribution to the sum and the progress of medical science.

"I see the widening of the limitless field of preventive medicine and public health, with physicians and public health nurses working hand in hand for the borning and the building of better human bodies and the development of better human minds.

"I see a medical and hospital campus around which a group of associated public and private hospitals will cluster, which will draw their resources of library, laboratory, and nursing service from the institution's abundant stores.

"I see the creation of an Institute of the Medical Sciences, grouping, under its administrative direction, the Medical School and the Colleges of Dentistry and Pharmacy, the School of Public Health and the special courses which prepare for the technical services of them all.

"I see a medical school, again, of so high ideals and so generous proportions that it will attract great teachers and draw great scholars, and train, in turn, great educators and scientific investigators and clinical leaders who will mold the movement of their time in modern medicine.

"I see a school whose graduates will be of so initial fitness, of so cultural preparation, of so thorough professional training that the University may fitly and unquestioningly set its seal upon them as a guaranty to the public that the health of mind and body, the issues of life and death, may be safely entrusted to their guiding hand.

"I see a profession, born of such a school, that shall rise above the strifes and jealousies of other days, that shall no longer tolerate mediocrity and commercialism in its midst, that shall rise to the full conception of its obligation of service, that shall awaken to that sense of social consciousness which will compel the full exercise of its educational functions for the benefit of the great mass of mankind, that will inspire and justify the public trust, that will make it the natural instigator and promoter of every measure for the

public good. May these things be in Minnesota!"

There is no doubt that Dr. Beard's vision inspired and stimulated Minnesota citizenry to bring forth its realization.

One of my great privileges at the University of Minnesota was to meet Dr. Beard in 1914, to be aided and encouraged by him as a junior member of the faculty, and later to enjoy an intimate friendship and professional relationship with him for the remainder of his life. He was deeply interested in tuberculosis and its control. In fact, in 1894 Dr. W. J. Mayo, president of the Minnesota State Medical Association, suggested that a committee be appointed to thoroughly consider the question of education concerning tuberculosis and report at the next annual meeting. Dr. Beard then introduced the following resolution: "Resolved, that a special committee be appointed by the president, to whom shall be referred the recommendation made in the president's address, and particularly those regarding the control of tuberculosis; that this committee be instructed to consider and report to the society at its next annual meeting such measures as it shall deem practicable for the control of tuberculosis; and further, that this committee be instructed to prepare or to select already prepared tracts, which shall convey in popular terms such information regarding the sanitary care of tuberculosis patients as may be placed wisely in the hands of the people, and to submit such tracts to the society for its approval at the next annual meeting."

Dr. Mayo appointed Dr. Beard chairman of such a committee and the report presented by him at the annual meeting in 1895 contained "statements concerning tuberculosis which the committee recommended for publication as instructive to the public of the position of medical science upon this important subject." One of the items for this proposed publication was "Tuberculosis, which in its several forms is destructive of a large percentage of the human race, is an infectious and preventable disease. It should be classed with scarlet fever, diphtheria and typhoid fever." Similar gems constituted the remainder of the proposed publication. This was followed by five resolutions containing such items as securing legislation to require reporting of cases to boards of health, laws and rules for isolation of tuberculous patients, and rigorous inspection of cattle to the extent that milk and meat from tuberculous animals be controlled and sterilization of their dairy products be practiced. The entire report of this committee can be read with profit today.

In the early 1920s, after completing a manuscript for a proposed book on tuberculosis for nurses, I mustered courage to ask Dr. Beard to read it and make corrections and clarifications. He graciously consented and devoted much time and work to its pages. At our first conference it was evident that the English of the original production was worse than had been suspected and that Dr. Beard's knowledge of many aspects of tuberculosis was superior to that of the author of the manuscript. In fact, the original copy had to be completely redone, after which Dr. Beard reread the entire manuscript and made corrections which had been overlooked. He then consented to write an introduction which in 1924, probably influenced the publisher's acceptance of the paper more than the chapter contents.

Between 1924 and 1932, Dr. Beard did similar meticulous reading of manuscripts of 6 other books, in addition to numerous papers which were published in nursing, medical, and educational journals. All of this, along with his helpfulness, encouragement, and many kindnesses, make impossible my adequate expression of appreciation and sincere esteem for Dr. Beard.

Following retirement from the school of medicine, Dr. Beard continued as chairman of the school of nursing committee and the committee on endowment. From 1925 to 1932 he was executive secretary of the Hennepin County Public Health Association. Throughout the years since 1907 when Dr. W. J. Mayo was first elected regent of the university, Dr. Beard was in close touch with the Mayo Clinic staff. He was a firm promoter of the Mayo Foundation, beginning his campaign in its support in 1914. He felt the crowning event of his life would be the writing of a complete history of the Mayo Clinic. The Mayos provided him with an office at the clinic and other needed facilities. There he spent the greater part of two years assembling historical material and writing. In late 1934 he returned to Minneapolis where he continued his book. Unfortunately, he had started too late. When the first 4 chapters were nearly completed, he began to develop symptoms of cerebral arterial sclerosis, after which he accomplished very little. He died from essential hypertension with arterial sclerosis Aug. 14, 1936, at the age of 80.

Concerning the history, Dean Lyon said, "If, as this writer suspects, this work is unfinished, we may be certain that this is due to Dr. Beard's unflinching pursuit of detail. Not one date, number, or smallest fact would be set down until after the fullest verification. He abhorred sketchy outline and summary. These traits demonstrate intellectual honesty of a high type."

In the book *The Doctors Mayo*, first edition,

page 716, October 1941, Miss Helen Clapesattle said, "I want to acknowledge my deep obligation to Dr. Richard O. Beard and Thomas E. Steward, whose work over a period of years in assembling materials and recording interviews enabled me to start with a body of valuable data already accumulated."

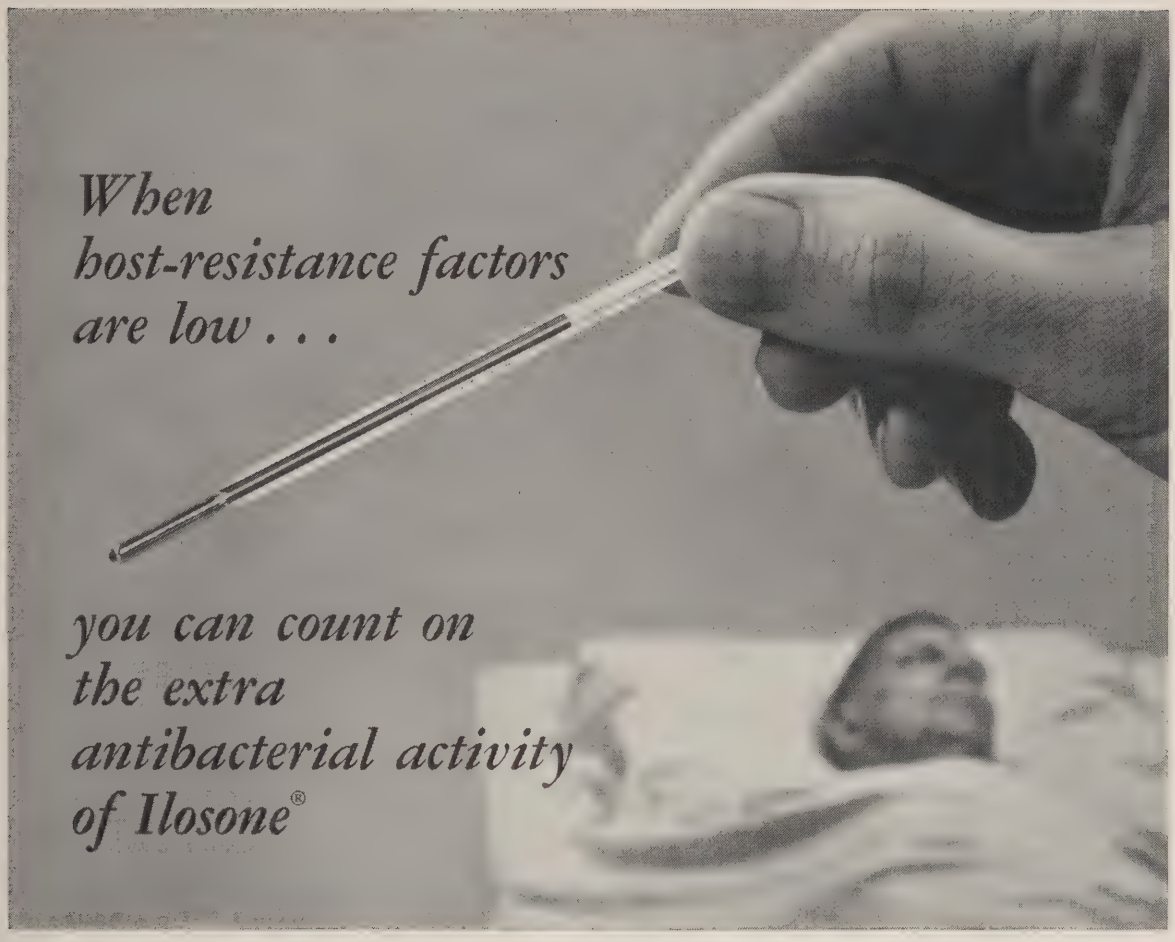
In a beautiful memorial published in *Minnesota Medicine,* October 1936, Dean Lyon wrote: "One day shortly before he died Dr. Beard eluded his attendant, got himself dressed, went by streetcar to the University, pursued his usual pathway to Millard Hall, followed its corridors so often trod by him and doubtless stopped to glance at old class pictures, nearly every individual in which he knew. He went to the Dean's office and talked for a time with Dr. Diehl. Here he was located by anxious friends and induced to go home to bed.

"This episode is emblematic of the man and illustrates his two great qualities, loyalty and enthusiasm. The prime object toward which these qualities were directed was the Medical School of the University of Minnesota. He was the last of the old wheel horses of that institution and one of its staunchest supporters."

Although the name of Richard Olding Beard is not engraved on any hall or in any prominent place on the schools of medicine and nursing campus, time can never erase the university's great indebtedness to him.

SIMULTANEOUS OCCURRENCE of ataxia-telangiectasia, abnormal thymus, immunologic deficiency, and malignant condition may stem from a common cause. High incidence suggests that this association is not coincidental. Patients may have genetic defect of a factor required for development of normal immunologic status. The relationship of the thymus to development of peripheral lymphoid tissue, immunologic capacity, and malignant tumors of lymphorecticular tissue indicates that thymic irregularity potentiates several aspects of the syndrome. All the components of ataxia-telangiectasia might stem from primary mesenchymal abnormality. Multiple immunologic abnormalities may result from a quantitative immunologic deficiency due to faulty thymic induction. Healthy mesenchyme is required for lymphoid development of the thymus. Ataxia in infants with the syndrome progresses to total incapacitation by adolescence. Telangiectasia appears when the patient is about 3 years old. Approximately 85% of patients have sinopulmonary infections that often are fatal. The thymus may be lacking or too small to detect or may show microscopic structural abnormalities. The bone marrow may lack plasma cells or the cells may be scanty. Antibody response and lymph node structure frequently are abnormal. Malignant tumors invade lymphoid tissue; necropsy may show generalized reticulum-cell sarcoma, Hodgkin's disease, or undifferentiated round-cell sarcoma.

RAYMOND D. A. PETERSON, M.D., WILLIAM D. KELLY, M.D., and ROBERT A. GOOD, M.D., University of of Minnesota, Minneapolis. Ataxia-telangiectasia. Lancet 1:1189-1193, 1964.



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Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

Before prescribing, consult package circular.

Book Reviews . . .

Surgery in World War II:
Activities of Surgical Consultants (Volume II)

Editor-in-Chief, COL. JOHN BOYD COATES, JR., *Vol. 2, 1062 pp., ill., Superintendent of Documents, Government Printing Office, Washington, D.C., 1964. $8.50*

This volume is one of a series published by the Medical Department of the United States Army describing its activities during World War II. The consultant group both before World War I and World War II was not a permanent department of the regular Army, and in both instances was activated following the onset of hostilities. Its role was to advise, supervise, and facilitate the rapid expansion of the medical corps to meet the needs of the armed services in the various theaters of war. The general organization was based on a chief surgical consultant who was immediately responsible to the director of professional services and, in turn, to the chief surgeon. Beneath the chief surgical consultant were senior consultants in general, plastic, orthopedic, neuro-, and chest surgery and anesthesia, transfusion and shock, urology, otolaryngology, ophthalmology, and radiology. Beneath the senior consultants were consultants working on the level of the Army, corps, divisions, hospitals, and base sections. Their role was to directly supervise the activities of the specialists carrying out the actual medical care. This particular volume deals entirely with the activities of the senior consultants and the chief consultant and, therefore, is devoted almost in its entirety to administrative problems of a rapidly expanding organization committed to establishing the highest quality medical care available to any army in the world.

The volume is comprised of the individual reports of the chief consultant and senior consultants in the European and Pacific theaters. The reports are written by the consultants, though in the third person, and are a compilation of information from official reports and from the personal diaries of the essayists. All the reports follow the same general outline and this has led to some rather tedious repetitions that might have easily been covered in one general section at the beginning of the book. Aside from this, the reports are written in a very personal manner. Many are dotted by reminiscences and anecdotes that pleasantly relieve the most straightforward presentation of factual data. I read with particular interest the sections written by Dr. Elliott Cutler, the chief consultant; Dr. Rober M. Zollinger, senior consultant of general surgery; and Dr. Loyal Davis, senior neurosurgery consultant, not only from the point of view of the organizational and surgical problems with which they dealt, but also for the great insight into the personal problems and conflicts of a practiced group of individualists forced to live under the same roof and occupy the same office space while trying to maintain, expand, or establish the

(Continued on page 18A)



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(Continued from page 16A)

independence, rights, or sovereignty of the various interest groups. It seems evident that some of the animosity generated during those times still rankles.

In general, the book could have been written in a much more concise fashion but conceivably would have lost some of its personal appeal. The illustrations are of adequate quality but at times have only a general interest value and add little to the factual information presented.

The volume will be of great interest to those who were in the medical corps during the Second World War, and to those who have acquaintanceship with any of the authors. It might also be of great interest to those involved in university teaching programs because in both first and second World Wars the consultant group was largely drawn from the major teaching centers. Medical students and those in the early years of specialization would probably find this book of little interest.

PETER A. SALMON, M.D.
Minneapolis

Animal Behaviour and Drug Action

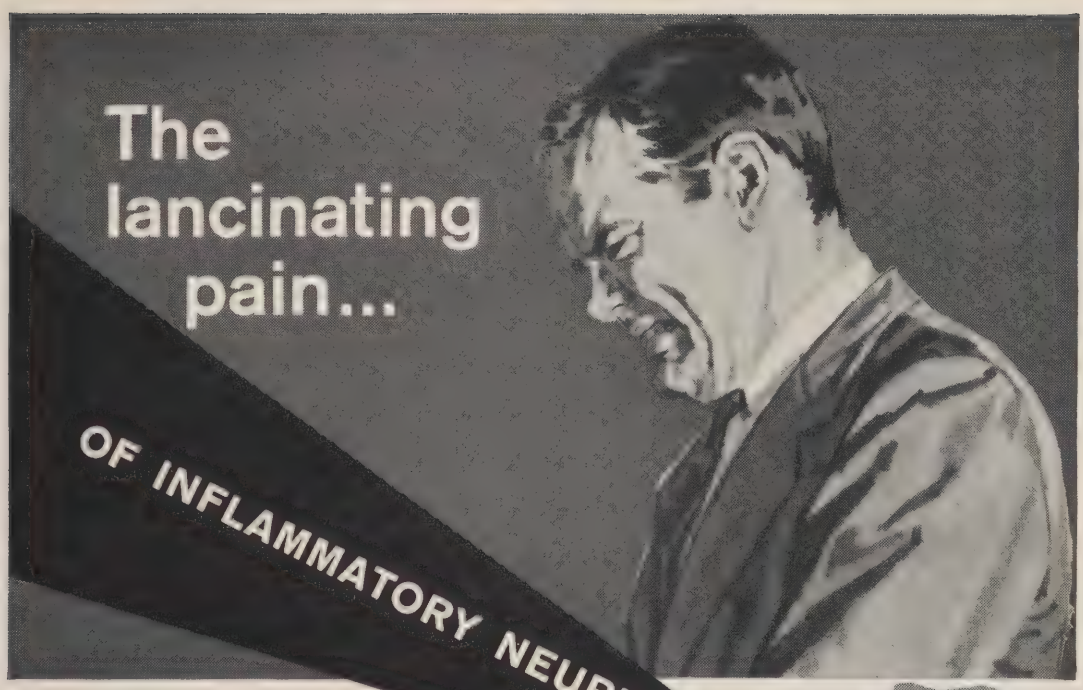
edited by A. V. S. DE REUCK *and* JULIE KNIGHT, *491 pp., ill., Little, Brown & Co., Boston, 1964. $13*

This publication of a symposium on "the role and limitations of animal behaviour studies in the investigation of drugs which affect the central nervous system" contains a wealth of information and interesting discussion. The redundancy common to symposia appears, in the present case, to be an asset frequently illuminating different facets of a given research area. The index is helpful and reasonably adequate in assembling information on the wide range of topics considered.

The session on factors modifying the behavioral effects of drugs in laboratory animals, and the general discussion on the standardization of experiments seem especially significant. The influence of factors such as heredity, previous experience, nutritional status, group composition, and test design on the behavioral response to drugs indicates the need for rigorous standardization and for the detailed publication of experimental conditions. It is unfortunate that only passing reference—prompted by Herxheimer's pertinent remarks on the need for controlling lighting—is made to the important findings of a circadian cycle in susceptibility to drugs as another variable to be controlled. These rhythms are of such general occurrence that one could expect most, if not all, behavioral phenomena to exhibit a circadian cycle in quality and intensity or both. This is already known in the case of gross locomotor activity, and very probably extends to the more complex patterns of social activity and to the more restricted responses of operant methods. Circadian system stages, defined by the phase relations among a set of physiological functions, should not be equated with a mere concern about "the initial base line or control level," discussed in relation to the so-called "law of initial value," which considers only the level of a given function under study, rather than the critical stages of the circadian system as a whole. One wonders in this context as to whether estimates of the spectra of the various rhythmic processes might not provide new end points to the pharmacologist, as is the case for the effect of reserpine on the variance spectrum for rectal temperature in the human.

The problems of determining the neurophysiological

(Continued on page 20A)



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References: **1.** Baker, A. G.: Penn. Med. J. *63*:697 (May) 1960. **2.** Smith, R. T.: New York Med. (Aug. 20) 1952, pp. 16-19. **3.** Smith, R. T.: Med. Clin. N. Amer. (Mar.) 1957. **4.** Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. (Nov.) 1955. **5.** Sforzolini, G. S.: Arch. Ophthal. *62*:381 (Sept.) 1959. **6.** Gile, J. H.: W. Virginia Med. J. *59*:120-122 (May) 1963.



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(Continued from page 18A)

and biochemical correlates of behavior, and the effects of drugs thereon, receive deserved attention in this book. The request for correlation on an individual and temporal basis presents a formidable challenge to the neurochemist. It will require the development of methods which would, for example, permit the monitoring of the neurohumoral content at specific brain sites while ongoing behavior is being investigated.

The absence of sufficient statistical information in several of the presentations is disconcerting, especially in those cases in which material is apparently being published for the first time.

WALTER NELSON, PH.D.
Minneapolis

NEW BOOKS RECEIVED

The Conditioning Therapies: The Challenge in Psychotherapy edited by JOSEPH WOLPE, ANDREW SALTER, and L. J. REYNA, 192 pp., ill., Holt, Rinehart and Winston, Inc., New York City, 1964. $7

Crossen's Synopsis of Gynecology by DANIEL WINSTON BEACHAM and WOODARD DAVIS BEACHAM, 6th ed., 371 pp., ill., C. V. Mosby Co., St. Louis, 1963. $7.50

The Retinal Vessels: Comparative Ophthalmoscopic and Histologic Studies on Healthy and Diseased Eyes by R. SEITZ, 186 pp., ill., C. V. Mosby Co., St. Louis, 1964. $14.50

Immunization Information for International Travel, 1963-64 prepared by the Epidemiology and Domestic Operations Branch, Division of Foreign Quarantine of the Bureau of Medical Sciences, U.S. Public Health Service, 98 pp., ill., Superintendent of Documents, U.S. Government Printing Office, Washington, D.C., 1964. 35c

The Medical Treatment of Peptic Ulcer by GEORGE GORDON MCHARDY, 78 pp., Charles C Thomas, Springfield, Ill., 1963. $4.75

Communicable and Infectious Diseases: Diagnosis, Prevention, Treatment by FRANKLIN H. TOP, 5th ed., 902 pp., ill., C. V. Mosby Co., St. Louis, 1964. $21

Common Complaints: Consultations in Medicine, a collection of medical articles from CONSULTANT magazine, 206 pp., ill., Smith, Kline & French Laboratories, Philadelphia, 1964. $3

The Advance of the Fungi by E. C. LARGE, 488 pp., ill., Dover Publications, Inc., New York City, 1962. $2.25

Medical Sociology and Cultural Anthropology of Sport and Physical Education by ERNST JOKL, 166 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $7.50

News Briefs . . .

North Dakota

DR. H. J. WEYERS has discontinued practice in the Medical Arts Building, Fargo, and is now associated with Drs. Robert L. Geston and Roy E. Kulland in the West Fargo Medical Center.

* * * *

DR. GALE R. RICHARDSON of Minot has been reelected president of the North Dakota State Society of Pathologists.

* * * *

DR. MARIANNE WALLIS of Minot has been elected president of the North Dakota Society of Radiologists. Dr. Wallis is a member of the American College of Radiology.

Other officers elected are Drs. Johannes H. Penners, Grand Forks, vice-president; Robert J. Olson, Williston, secretary; and H. Milton Berg, Bismarck.

* * * *

DR. ROY W. FRICKE, internist at the Quain and Ramstad Clinic, Bismarck, has been certified by the American Board of Internal Medicine. Dr. Fricke received his M.D. degree from Vanderbilt University in 1958 and joined the clinic in 1962. He also is on the staff of Bismarck and St. Alexius hospitals.

* * * *

DR. JOSEPH D. CRAVEN of Williston has assumed presidency of the North Dakota State Medical Association, succeeding Dr. G. Alfred Dodds of Fargo. Dr. Cravens is a 1937 graduate of the Stritch School of Medicine of Loyola University, Chicago, and a member of the American Academy of General Practice.

* * * *

Dr. G. W. Toomey of Devils Lake was named president-elect of the state group. Other officers are Drs. Verrill J. Fischer, Minot, first vice-president; Clifford H. Peters, Bismarck, second vice-president; Lee A. Christoferson, Fargo, speaker; Philip O. Dahl, Bismarck, vice-speaker; William M. Buckingham, Bismarck, secretary; and Richard D. Nierling, Jamestown, treasurer.

* * * *

Two physicians, Drs. Frank M. Melton of Fargo and Charles A. Hamilton of Bismarck, have been named fellows of the American College of Physicians. Dr. Melton, dermatologist at the Dakota Clinic, Fargo, was graduated in 1939 from the University of Louisville School of Medicine, Louisville, Ky. Dr. Hamilton, a specialist in cardiovascular disease, is a graduate of Harvard Medical School, Boston, a diplomate of the American Board of Internal Medicine, and a member of the American College of Chest Physicians.

Minnesota

DR. HOWARD B. BURCHELL, professor of medicine at the Mayo Graduate School of Medicine of the University of Minnesota at Rochester and a consultant in medicine at the Mayo Clinic since 1940, has been named editor of *Circulation,* monthly scientific journal of the American Heart Association. Dr. Burchell assumes the editorial post with the January 1966 issue.

Assisting as associate editors will be Drs. Patrick A. Ongley, associate professor of pediatrics, and Ralph E.

(Continued on page 22A)



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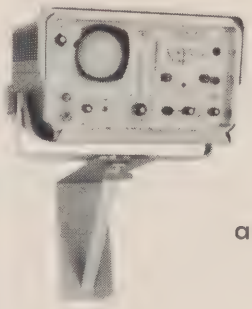
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NEWS BRIEFS

(Continued from page 21A)

Smith, assistant professor of medicine, both at Mayo Graduate School of Medicine.

Active in AHA since 1948, Dr. Burchell served on the National Advisory Heart Council from 1958 to 1962 and on the editorial board of *Circulation*. The association gave him its national award of merit in 1958, and a Minnesota award in 1959.

* * * *

DR. VINCENT L. GOTT, University of Minnesota-trained heart surgeon, has been appointed head of heart surgery and associate professor at Johns Hopkins University, Baltimore. Dr. Gott, a 1953 graduate of Yale University School of Medicine, interned at University of Minnesota Hospitals in 1953 and 1954, then remained on the staff as a resident and postgraduate fellow.

* * * *

DRS. MILTON ALTER and KENNETH F. SWAIMAN of the University of Minnesota have received more than $10,000 in research grants from the Epilepsy Foundation. Dr. Alter will go to Israel in August to study geographical, cultural, and racial factors in epilepsy. Dr. Swaiman will study the effect of one of the B vitamins on children with convulsive disorders.

* * * *

DR. ROBERT I. GRUYS of Wells has been named a fellow of the International College of Surgeons. Dr. Gruys received his degree in 1947 from the University of Minnesota Medical School.

* * * *

DR. AMBROSE E. SPRAFKA of Detroit Lakes has opened a three-day-a-week practice at the community clinic in Brown Valley. Dr. Sprafka was graduated in 1937 from the University of Minnesota Medical School and completed his internship in Chicago.

* * * *

DR. OLIVER H. BEAHRS, head of the Mayo Clinic section of surgery, has been elected president of the American Society of Head and Neck Surgeons. Dr. Beahrs, a 1942 graduate of Northwestern University Medical School, Chicago, is a member of the American College of Surgeons, the Central Surgical Association, and the Western Surgical Association.

* * * *

DR. EARL T. CARTER, Mayo Clinic specialist in preventive medicine, has received the Walter M. Boothby Award for outstanding research in promotion of health and prevention of disease in professional airline pilots. Dr. Carter is a 1948 graduate of the Northwestern University Medical School, Chicago, and a member of the Aerospace Medical Association, which made the award.

* * * *

DR. ABBOTT SKINNER has been elected president of the medical staff of Charles T. Miller Hospital, St. Paul. Dr. Skinner, a general surgeon, is a 1942 graduate of Harvard Medical School, Boston. He is a member of the American College of Surgeons.

Other officers elected are Drs. John B. Coleman, first vice-president; Philip H. Soucheray, second vice-president; and Albert F. Hayes, chairman of education and research.

* * * *

DR. ROBERT J. WHITE, director of neurosurgery at the Cleveland Metropolitan General Hospital, has received a plaque from the College of St. Thomas in recognition of his contribution to medical research. Dr. White developed the first isolated brain preparation, enabling investigators to study the brain of a monkey as a totally

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isolated organ under various normal and pathological situations. Before receiving his degree from Harvard Medical School in 1953, Dr. White attended the premedicine program at St. Thomas from 1946 to 1949 and received his bachelor of science degree from the University of Minnesota in 1951 and the doctorate of philosophy from the same institution in 1962.

° ° ° °

Seven new consultants have been appointed to the staff of the Mayo Clinic, Rochester. Coming from the residency staff of the Mayo Graduate School of Medicine of the University of Minnesota are Drs. Allan J. D. Dale, neurologist, graduate of the University of Manitoba, Winnipeg; Keith E. Holley, experimental and anatomic pathologist, graduate of the Loma Linda University School of Medicine, Loma Linda-Los Angeles, Calif.; Panayotis P. Kelalis, urologist, graduate of the National University of Ireland; and Ben D. McCallister, internist, graduate of the University of Kansas School of Medicine, Laurence-Kansas City, Kan.

Other appointees are Dr. Harry F. Bisel, clinical oncologist, graduate and former assistant professor of medicine, University of Pittsburgh School of Medicine; Dr. Manuel R. Gomez, pediatric neurologist, graduate of Universidad de la Habana Facultad de Medicina y Farmacia, Havana, Cuba, and lately assistant professor of neurology at Wayne State University, Detroit; and Dr. Frederic C. McDuffie, microbiologist, graduate of Harvard Medical School, Boston, and lately associate professor of medicine, University of Mississippi School of Medicine, Jackson.

° ° ° °

DR. LOWELL L. HENDERSON, consultant in medicine in the Mayo Clinic, Rochester, has been elected president of the American College of Allergists.

South Dakota

A seven-man medical board has been created by Governor Nils Boe to advise and counsel the state motor vehicle department in connection with driving privileges of persons with physical or mental impairment. Board members are Drs. Lawrence G. Behan, Yankton; Robert R. Giebink, Sioux Falls; Robert C. Jahraus, Pierre; George W. Smith, Sioux Falls; John J. Stransky, Watertown; William R. Taylor, Aberdeen; and Charles E. Tesar, Rapid City.

° ° ° °

DR. RICHARD I. PORTER has joined the staff of the Yankton Clinic, Yankton. Dr. Porter, 28, received his medical degree from Washington University, St. Louis, Mo. He practiced for a short time in Graceville, Minn., coming to Yankton in March.

° ° ° °

DR. STERLING BERG of Tyndall has been elected president of the medical staff at St. Michael's Hospital in that city. Other officers are Dr. Glenn Kleinsasser of Scotland, vice-president, and Dr. Alan H. Domina of Tyndall, secretary-treasurer.

° ° ° °

DR. WILLIAM E. DONAHOE, Sioux Falls physician and pioneer in community health programs in that area, has received the College of St. Thomas Aesculapian Club Award. The award is given annually to an alumnus of St. Thomas by students in premedicine and biological science at the St. Paul college in recognition of com-

(Continued on page 24A)

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WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED—Locum tenens—Pediatrician for one year, Multi-specialty group, northern Minnesota. Salary open. Northwestern Clinic, Crookston, Minnesota.

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WANTED—1 or 2 general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D. Greenbush, Minn.

NEWS BRIEFS

(Continued from page 23A)

munity service. In 1920 Dr. Donahoe introduced Sioux Falls' first diphtheria immunization program and established the first free children's clinic. He also organized and served as president of the state's first health officers' association.

Deaths . . .

DR. ROLF HOVDE, 72, physician and surgeon in Winthrop, Minn., for forty-six years, died April 10. Dr. Hovde was born in Brookings, S.D. In 1917 he received an M.D. degree from the University of Minnesota and began practice in Winthrop in 1919. Dr. Hovde was a member of the American Academy of General Practice, the American Association of Railway Surgeons, and national, state, and county medical societies. He served on the staffs at Union and Loretto hospitals, New Ulm, Minn., at Arlington Municipal Hospital, Arlington, Minn., and Glencoe Municipal Hospital, Glencoe, Minn. In appreciation of his many contributions to community life, the citizens of Winthrop declared June 26, 1963, "Dr. Rolf Hovde Day," and presented Dr. Hovde a gold-plated stethoscope.

* * * *

DR. HENRY CARL OTTO, 80, died April 27 in Detroit Lakes, Minn. A resident of Frazee, Minn., for fifty-six years, he practiced medicine in the Frazee-Vergas area after graduating from the Louisville and Hospital Medical College, Louisville, Ky., in 1908. Dr. Otto was a member of the American Academy of General Practice and national, state, and county medical societies.

* * * *

DR. FRITHIOF L. KLING, 87, who had formerly practiced medicine at Milaca, Minn., from 1918 until his retirement, died April 19, in Minneapolis. Dr. Kling received his degree from the Minneapolis College of Physicians and Surgeons, Minneapolis, in 1903.

* * * *

DR. ARTHUR W. GARBRECHT, 71, physician and surgeon in St. Paul since 1924, died April 8 in that city. Born in Berlin, Germany, Dr. Garbrecht received his degree from Friedrich-Wilhelm-Universitat Medizinische Fakultat, Berlin, in 1921. He was a member of the Radiological Society of North America and of national, state, and county medical societies. He was a staff member at Riverview Memorial Hospital, St. Paul.

* * * *

DR. BURTON I. ROSENHOLZ, 68, died April 23. A native of St. Paul, Dr. Rosenholz was graduated from the University of Minnesota Medical School in 1921 and practiced in St. Paul from 1925 until his retirement in 1952. He was a member of the American Board of Pediatrics.

* * * *

DR. JOHN A. O'HANLON, 59, died in Minneapolis on May 14. Dr. O'Hanlon was graduated from Marquette University School of Medicine, Milwaukee, in 1933. He had been in private practice in Minneapolis since 1949 and had been chief medical officer of the Minneapolis post-office since February 1964. Dr. O'Hanlon was a member of the American Academy of General Practice.

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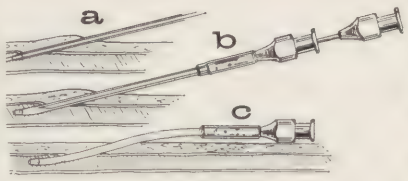
DR. THOMAS E. FLINN, 80, who practiced in Redwood Falls, Minn., from 1911 to 1946, died there on April 8. Dr. Flinn was graduated from Rush Medical College, Chicago, in 1909. He served as a major in the United States Army Medical Corps in World War I.

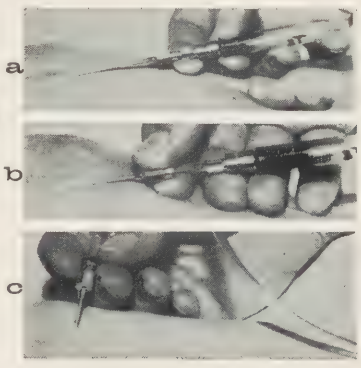
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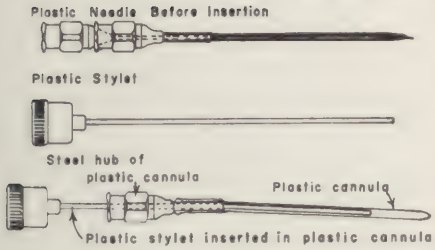




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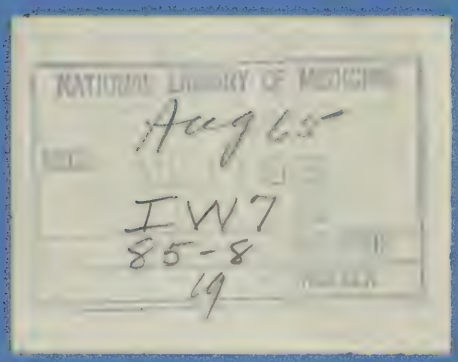
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1. Nelson, L. S., and Stoesser, A. V.: Ann. Allergy, *22*:527, 1964.

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*Monti, A. A. F.: Rev. Bras. Cir. 43:288-297 (Apr.) 1962.

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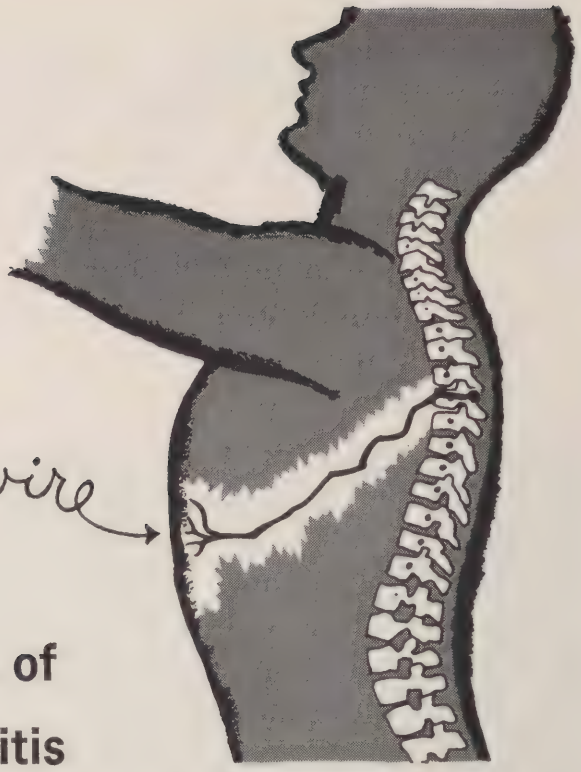
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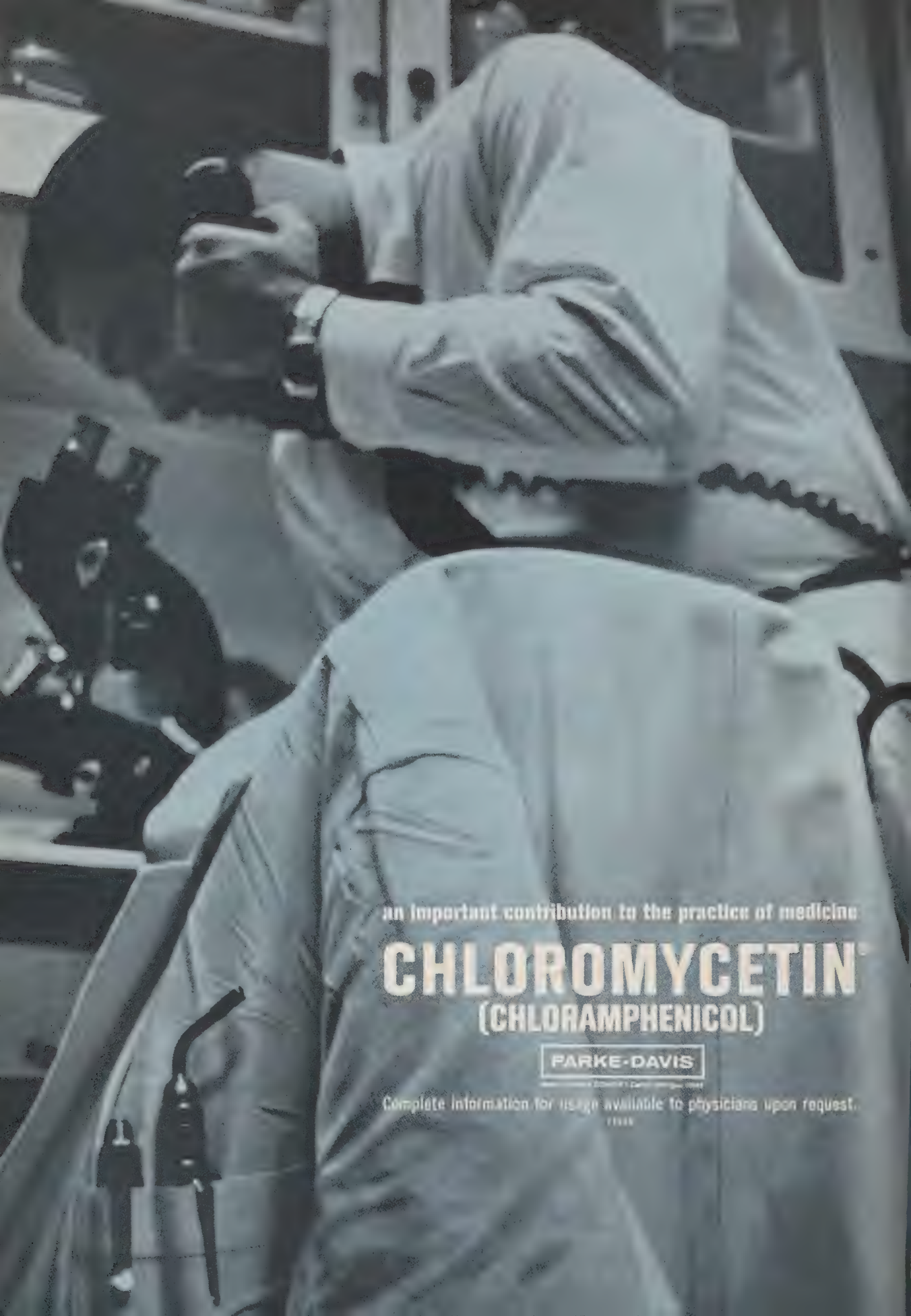
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Articles and features to be found in the next issue of THE JOURNAL-LANCET

Throughout the past years rapid developments in coagulation research have produced a burgeoning and complicated mass of information about the coagulation system in man. This first sentence from the article "A Simplified Approach for the Detection of Coagulation Disorders," by William Krivit, M.D., and James G. White, M.D., Minneapolis, is a factual statement of the reason the authors undertook the leading article in the September issue of THE JOURNAL-LANCET. In the article they outline how a practitioner can determine, directly and simply, whether his patient has a coagulation deficiency. Included is a most informative chart relating the sequence of procedures to the clinical findings.

Another article that helps to clarify a confusing situation is "Cutaneous Manifestations of Some Internal Diseases," by Carl W. Laymon, M.D., Minneapolis. Clinical professor of dermatology at the University of Minnesota and director of the department of dermatology at the Hennepin County General Hospital, Dr. Laymon follows McCleary's classification of cutaneous xanthoma and discusses each entry from the standpoint of diagnosis, treatment, and prognosis.

In the article, "Some Present-Day Problems in Infectious Heart Disease," by Joseph E. Geraci, M.D., of the Mayo Clinic, the antibiotic prophylaxis and treatment of streptococcal infections, rheumatic fever, bacterial endocarditis, and infections of the pericardium are reviewed.

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1. Griffith, R.S., and Black, H.R.: Current Ther. Res., *6:* 253, 1964.

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Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

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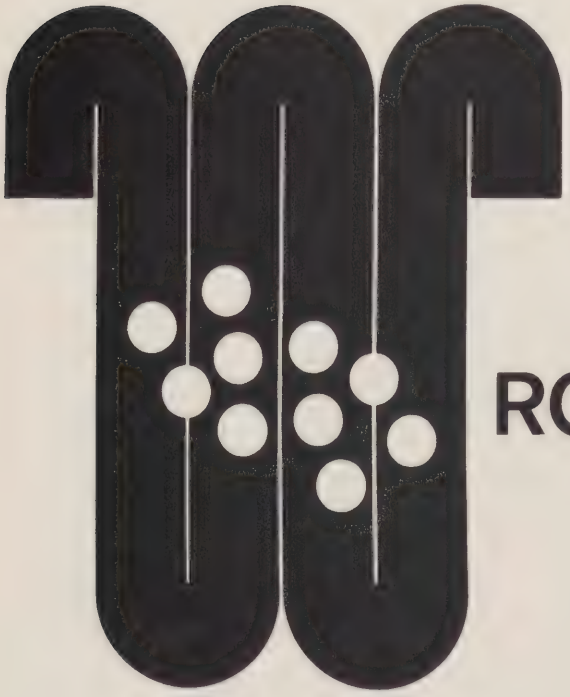
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Series on ALLERGY *for the* PRACTITIONER

Fifty Ways To Diagnose Allergy

KENNETH J. JOHNSON, M.D.

Bismarck

If we don't think of or look for allergy we will usually fail to diagnose it. Similarly, if we think of the concept of allergy or hypersensitivity but don't know how to recognize it or test for it, we likewise will fail to diagnose it. In order to help others diagnose allergy when it is present, I offer the following list of methods which have been advanced by allergists to determine the presence of an allergic condition. Some are widely accepted and familiar to many; a few are not widely accepted. Some can easily be used in a general practice, while others are so technical only a specialized laboratory can perform them. Some are widely applicable, others very limited in their use. Some are old, some are new. Nevertheless, I believe all are interesting and worth knowing.

Because of space limitations, each description tends to be oversimplified. Only one reference can be given for one piece of information, but that one usually will lead the reader to others. No claim is made that this is a complete list. May I point out that a conclusive diagnosis should not be made on the basis of only one of the following methods, for several are necessary. Every patient should have the benefit of a thorough survey of his past personal and family history, including that of his children, and thorough physical and laboratory examinations.

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These 50 items are classified in groups: history and physical findings, cell studies, skin tests, ingestion studies, blood chemistry determinations, serum binding, and therapeutic trials.

HISTORY AND PHYSICAL FINDINGS

1. *History.* Because the allergic diathesis manifests itself throughout life, and often with a different manifestation at each period of life, the typical atopy patient will have had more than one allergic disease. The commonest sequence is eczema in infancy, hay fever in childhood, and asthma in adulthood. Because atopy is hereditary, the members of the family—grandparents, parents, uncles, aunts, siblings, children—should have had allergies also. These are corroborative evidence of allergy in the patient.

2. *Stigmata.* Allergic shiner, darkening of the lower orbitopalpebral grooves; allergic salute, mannerism of rubbing hand against nose; transverse nasal crease, the deformity resulting therefrom; and nose and mouth wrinkling, mannerisms which relieve itching, are commonly found in children with allergic rhinitis.[1]

3. *Nasal mucosa inspection.* The nasal mucosa appears boggy and gray in allergic rhinitis, and the nasal discharge is thin and watery. A nasal polyp is diagnostic of allergy. This edema of the nasal mucosa is the earliest and commonest expression of increased capillary permeability in allergic disorders of the nose. It often results in epistaxis.[2]

4. *Inspection of skin.* Dermatitis due to allergy is characterized by erythema, vesicles, and often crusts, commonly called eczema, in a characteristic distribution—usually flexural in atopic dermatitis and over the area of contact in contact dermatitis.[3]

5. *Wheal.* Wheals invariably are an allergic manifestation due to hematogenous distribution of antigen to the skin.[4]

6. *Angulus asthmaticus.* The presence of musical expiratory rales on auscultation of the chest is typical of a bronchial asthma paroxysm.[5] However, according to Gutman,[6] objective evidence of asthma may be established between attacks by auscultation in the angle between the clavicle and the medial head of the sternocleidomastoid muscle at the manubrium sterni in the supraclavicular fossa. He calls this area the angulus asthmaticus or asthma auscultation point.

7. *Bedside ventilatory test for asthma.* A forced expiration while lying supine will induce an asthmatic wheeze which can be auscultated by stethoscope during the quiescent period in most patients.[7]

8. *Nebulizer provocative testing.* Determining the vital capacity, timed vital capacity, and maximal expiratory flow rate before and after 10 breaths of a nebulized solution of wool—100, 1,000, or 10,000 protein nitrogen units per cubic centimeter, depending on response—demonstrated a decrease in pulmonary function and caused wheezing and dyspnea in patients allergic to wool.[8] Bernstein,[9] using other allergens by this method, found pulmonary flow resistance to be the most reliable objective index. Tuft and associates[10] stated that typical atopic dermatitis lesions in a susceptible patient may be induced by inhalation of micronized, powdered, house-dust allergen, thus demonstrating the cause.

9. *Intravenous histamine test for asthma.* Intravenous saline injection as a control, followed by rapid intravenous injection of 0.03 mg. of methacholine chloride, is a simple objective screening procedure for diagnosis of bronchial asthma. Serial vital capacity determinations are done one-half and one minute later and repeated until the value returns to the base line. Auscultation and questioning regarding subjective symptoms will corroborate the diagnosis. Reduction of 11% or more in the vital capacity after histamine or methacholine or both injections indicates a positive reaction. While a positive response does not establish the diagnosis—a few patients without pulmonary involvement may have positive responses—a negative response helps rule out asthma. Cardiac arrhythmia, marked hypertension, or presence of asthmatic paroxysm are contraindications to the test.[11]

10. *Acceleration of the pulse.* Coca[12] states that an allergic reaction to a food causes acceleration of the pulse (familial nonreaginic food allergy or idioblapsis). This method of diagnosis is very long and tedious and is not accepted by many allergists.[13]

11. *Cystoscopy.* A food allergy may cause edema of the urinary bladder wall (analogous to a wheal on the skin), noted in cystoscopy as a thickening. Biopsy of the wall shows eosinophils perfused in the wall with edema.[14]

CELL STUDIES

12. *Nasal swab.* Gently rubbing the floor of the nose and smearing the swab on a glass slide and staining with Wright's and Hansel's stains reveals goblet cells and eosinophils. These are diagnostic of allergic rhinitis.[15] Unger[16] has found that 80% of "sinus cases" are allergic, as confirmed by finding 4 to 100% eosinophils in the nasal smear after blowing the nose on a piece of cellophane.

13. *Sputum eosinophilia.* Sputum eosinophilia up to 100% is diagnostic of allergy or lung cancer or cancer of the trachea.[17] Bronchial asthma produces sputum with glairy mucus and Curschmann's spirals. Charcot-Leyden crystals and eosinophils are evident under the microscope.

14. *Urinary sediment eosinophilia.* In an allergy of the genitourinary tract, a Wright's stain of the urinary sediment may show many eosinophils.[18]

15. *Fecal eosinophilia.* Demonstration of eosinophils in the mucus adhering to the feces gives diagnostic evidence of gastrointestinal allergy.[19] The fresh mucus is dried on a slide and may be stained with May-Grünwald stain for thirty seconds, then diluted with distilled water and let stand another thirty seconds.[20]

16. *Blood eosinophilia.* Although not pathognomonic, the presence of eosinophilia in the blood is an important diagnostic point in allergic individuals.[21] In the morning, the eosinophil count drops in healthy persons and rises in asthmatic individuals.[22] Histamine injection causes eosinophils to increase in number in most allergic individuals but to drop in nonallergic persons.[23]

17. *Leukopenia.* Leukocytes undergo lysis in allergic patients; allergens demonstrating this have been shown to include ragweed, egg albumen, pollen, and house dust.[24] Leukopenia is too inconsistent, however, to be of much help in food allergy.[25]

18. *Basophil degranulation test.* Shelley[26] has shown that the blood basophil undergoes degranulation during the antigen-antibody reaction and permits the detection of specific sensitivity in a wide range of human allergic diseases. In this test, rabbit basophils are placed on slides prestained with neutral red to which serum from the subject is added and then challenged with specific antigen. Friedlaender and Friedlaender[27] point out that this test is not completely accurate because of many technical and theoretical problems.

19. *Supravital staining.* Nuclear staining of leukocytes by neutral red occurs in dead or dying cells. Addition of ragweed antigen to the blood of ragweed-sensitive individuals in vitro produces a significant increase in the number of neutral red-stained leukocytes when compared with the number stained when no antigen is added.[28]

20. *Vaginal eosinophilia.* A vaginal discharge with a high eosinophil count has been reported.[29] It is apparently secondary to an allergic reaction elsewhere in the body, such as hay fever, or to topical application of creams, jellies, or contraceptives.

21. *Tissue biopsy.* Persistence of antigen in almost any tissue (usually the skin) may cause dense infiltration of eosinophils with eventual necrosis surrounded by radially arranged epithelioid cells, as shown by biopsy of the allergic granule or nodule. Most of these patients had antecedent asthma, all have an allergic history.[30]

SKIN TESTS

22. *Conjunctival test.* Dropping a small pinch of dry pollen grains into the conjunctival sac causes redness and itching of the conjunctival membrane. This positive reaction may be controlled by the use of epinephrine and cocaine eye drops. Since the conjunctiva is a shock organ in hay fever, the reaction is more closely related to the actual clinical sensitization than is the reaction in the dermal tests.[31] However, this test is limited to only two suspected allergens at a sitting, since there are only two eyes to test. When hay fever clears, the dermal test remains the same while the eye test seems to become less positive.[32]

23. *Intradermal test.* Injection of sterile allergen extract of suitable dilution intradermally yields an erythema and wheal in ten to fifteen minutes if the subject is allergic—that is, if he has developed reagins to that specific allergen. Intradermal skin tests possess a high degree of reproducibility.[33] However, epinephrine 1:1,000 and a tourniquet must be at hand because of the danger of prompt generalized reaction to the antigen. Penicillin hypersensitivity may be predicted by intradermal skin test, using penicilloyl-polylysine.[34]

24. *Scratch test.* A ⅛-in. scratch on the skin, not deep enough to draw blood, followed by a drop of extract of specific allergen in 1:10 dilution, will produce an erythema or wheal in ten to fifteen minutes if the subject has developed reagins to that allergen. These tests are less sensitive than intradermal techniques but are not as dangerous. They are most accurate for pollens, least accurate for foods, in respect to correlation with clinical history.[35]

25. *Patch test.* The allergen suspected of causing the dermatitis is applied to a small piece of gauze, covered with a larger piece of waxed paper, applied to an uninvolved area of skin, and held in place with nonirritating tape for one or two days. It is tricky to get the right concentration of allergen—too much irritates even normal skin and too little will give a false-negative result. A table listing nonirritating concentrations of common chemicals for use in patch testing is given by Sulzberger and Baer.[36] Adrenocorticotrophic or steroid hormones do not effect immediate-type skin reactions to pollen extracts but do lessen the erythema and induration of delayed type patch test reactions. On the other hand, antihistaminics suppress the immediate reaction of scratch or intradermal skin tests but seem to have little or no effect on the delayed or patch tests.[37]

26. *Scratch-patch test.* When a patch test was negative using the drug suspected as being the cause of urticaria and a scratch test showed an inflammation in both patient and control subject, Gottlieb[38] used a scratch-patch test. The scratch was sufficient to draw blood; over this was placed a 1-cm. square of white blotting paper saturated with the drug. Two hours later generalized itching and wheals developed. The patch was removed the next day and showed swelling and erythema at the site.

27. *Photopatch test.* The chemical suspected of causing photosensitivity is applied by patch test near a control patch; after it is removed, light—Kromayer lamp with filter or a mercury arc lamp—is applied to the site of the test patch only. The control patch then is removed and the control site covered with light-impervious material. A positive test yields erythema and swelling at the test site within twenty-four hours.[39]

28. *Iontophoresis.* A method of skin testing also exists wherein the allergen is caused to penetrate the skin through sweat glands by an electric

current and the reaction read on the skin the same as for other skin tests.[40] This method results in fewer positive tests and requires special apparatus but involves no needles or scratches.

29. *Provocative food skin test.* Intracutaneous injection of a potent food extract will produce allergic symptoms—headache, nausea, nasal congestion, wheezing—according to Willoughby and associates.[41]

30. *Passive transfer.* A small amount of the patient's serum is injected intracutaneously into a series of sites on the back of a healthy young adult. A few days later the suspected allergens in proper dilution are injected into these sensitized sites. Each test is controlled by a similar injection into nearby nonsensitized skin, a positive test being one where the wheal is larger in the sensitized site.[42] This method of skin testing provides an excellent control and can be used for infants or for dermatitis patients whose skin can't be tested. It is a complex procedure, however, and may cause homologous serum hepatitis in the healthy person.

31. *Passive cutaneous anaphylaxis.* If 0.1 cc. of undiluted serum containing antimilk antibody from a patient allergic to milk is injected intradermally into a guinea pig, followed by intravenous injection of 0.5 cc. 1% Evans' blue dye and then milk albumen, a blue spot appears at the site of antibody injection.[43] This passive cutaneous anaphylaxis is due to the local antigen-antibody reaction that releases histamine and causes locally increased vascular permeability which allows the blue dye to collect and color the skin.

INGESTION STUDIES

32. *Aspirin test.* The best test for aspirin sensitivity as the cause of asthma is to have the patient hold a suspension of the drug in his mouth for a few minutes. If dyspnea does not increase within five minutes, the drug may be administered.[44]

33. *Diet and food diary.* If a food is suspected of causing allergic symptoms, one reliable method of proving this is to have the patient avoid the food completely (it may take fourteen days of total abstinence from this food) and to note disappearance of the symptoms. The food is then eaten liberally at each meal for up to three days to see if symptoms return. To be certain the recurring symptoms are not coincidental the elimination diet and provocative diet may be repeated.[45]

34. *Double gastrointestinal X-ray study.* An X-ray of the stomach and small intestine with barium medium alone to serve as a control is followed by the same study using the suspected allergic food incorporated in the barium mixture. If the patient is allergic to that food so that it causes flatulence, abdominal pain, diarrhea, or nausea, the second film will show gastric retention, hypermotility, and hypertonicity of the small bowel, with puddling, segmentation, and narrowing of the barium.[46] However, if other symptoms occur—asthma, angioneurotic edema, or neurodermatitis—motility is normal after ingesting the allergenic food.[47]

BLOOD CHEMISTRY DETERMINATIONS

35. *Blood histamine.* In healthy persons, no significant change occurs in the blood histamine after specific physical exercise; in patients with hay fever and asthma, however, an increase in blood histamine occurs within five to ten minutes.[48] A commercial laboratory can determine blood histamine on 11 ml. oxalated blood to which 50 mg. sodium fluoride are added.

36. *Electrophoresis.* Vaccarezza,[49] using electrophoretic paper strip technique, found the alpha-1 fraction of the serum to be decreased and the beta fraction, containing reagins, to be increased in patients with allergic rhinitis and asthma. He also found these patients had decreased plasma sodium and plasma chloride and increased potassium values. All 5 values showed highly significant statistical differences from those in healthy persons.

37. *Serum histaminopexy.* Normal human serum contains a specific gamma globulin (plasmapexin I) which binds histamine; in allergic serum, this protein is either absent or inactive.[50] Of the several ways to demonstrate this effect, the one most likely to be available to a small laboratory seems to be the method of Huriez and associates.[51] With this technique, histamine is bound on polystyrene particles. When normal human serum is incubated with this, agglutination occurs; allergic serum fails to agglutinate the particles.

SERUM BINDING

38. *Hemagglutination.* A way of predicting whether a patient will develop serum sickness from tetanus antitoxin has been found. Arbesman and co-workers[52] report that only those patients who had a hemagglutination titer of 160 or greater before injection of tetanus antitoxin developed serum sickness.

39. *Polystyrene.* Serum will bind the specific antigen; several methods have been devised to demonstrate this. Thus, grass pollen constituents

coupled to polystyrene can act as absorbant for allergic serum to cause aggregation.[53]

40. *Tanned-cell technique.* The tanned-cell technique of Boyden[54] causes aggregation of erythrocytes first treated by tannic acid to facilitate the adsorption of antigen and then incubated with the specific antiserum.

41. *B.D.B. technique.* Ragweed pollen constituents may be coupled by way of stable covalent azo bonds (bisdiazotized benzidine, or B.D.B.) to erythrocytes incubated with the patient's antiragweed serum, which causes aggregation.[55] On the other hand, Johnstone[56] found no significant difference in titer of hemagglutinating antibody between allergic and healthy persons when the B.D.B. method was used for testing eggs, milk, wheat, peanuts, or chocolate.

42. *Fluorescence.* Specific antibodies against ragweed antigen can be absorbed onto washed pollen grains and their presence demonstrated by exposure of the pollen to a fluorescein-conjugated antiglobulin globulin.[57] Millman and associates[58] detect antibody to rye grass by similar detection of fluorescence.

43. *Radioactivity.* I^{131}-labeled ragweed antigen is added to 0.5 cc. of 1:10 dilution of serum from a patient sensitive to ragweed. Antigen and serum are then incubated, and enough rabbit antihuman gamma globulin is added to precipitate all the human gamma globulin. The mixture is incubated again and centrifuged. The precipitate shows radioactivity to demonstrate the binding of the ragweed antigen by the antiragweed antibody in the patient's serum.[59]

44. *Gel diffusion.* The antigen to which the patient may be allergic and rabbit serum with antibody against this antigen are placed in two separate spots in an agar gel medium. When these diffuse through the agar and meet, the antigen-antibody complex precipitates to form a band or a line easily visible by reflected light. This method has been used for diagnosis of Caddis fly allergy with the patient's serum used instead of rabbit serum.[60]

THERAPEUTIC TRIALS

45. *Elimination test.* The substance under suspicion—inhalant, contactant, or ingestant—is eliminated from the patient's environment and improvement follows.[61]

46. *Antihistamine trial.* Benefit from antihistamines is unpredictable. Other actions of the drugs may relieve nonallergic disease. Extensive therapeutic trial is questionable,[62] although in specific instances they are of use. Raymond[63] found that symptoms of glaucoma produced or exacerbated with intradermal skin test were cleared by intravenous injection of calcium gluconate and an antihistamine (Phenergan®), and Powell[18] found a long-acting antihistamine to be a screening diagnostic aid in food allergy.

47. *Epinephrine trial.* Edema in a confined space readily produces painful discomfort. It is probably of allergic origin if a dramatic response to epinephrine occurs with a marked reduction in symptoms and signs. This may be the situation in certain cases of swelling of the fingers and their joints,[64] gastrointestinal allergy,[25] renal colic,[65] cystitis,[66] or glaucoma.[63]

48. *Steroid hormone trial.* Administration of a steroid hormone will control symptoms of allergy by depressing the immunologic responsiveness of the reticuloendothelial system.[67] Sherwood and Epstein[68] advocate triamcinolone for asthma, contact dermatitis, urticaria, hay fever, and perennial rhinitis.

49. *Immune serum trial.* Human immune serum from nonatopic persons who had been given injections of ragweed pollen may give relief to patients suffering from ragweed pollinosis.[69]

50. *Propeptan trial.* Propeptans are preparations derived from individual proteins through digestion by hydrochloric acid, pepsin, and trypsin, containing peptones, subpeptones, peptides, and amino acids but no native proteins. The propeptan from a specific food which is fed forty-five minutes before a meal of that food prevents the appearance of food-allergy symptoms.[70]

SUMMARY

Fifty methods of diagnosing allergy are very briefly presented. The techniques are of varying degrees of availability or value to the physician. No one method should be relied on exclusively: a conclusive diagnosis should rest on several methods.

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Effect of Hydrocortisone on Histamine-Induced Gastric Hypersecretion

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THE INITIAL WORK from the laboratory of Gray[1,2] showed the corticords to have a profound gastric secretagogue activity. At the time this threw much light on the phenomenon of stress ulcer. Subsequent investigation, however, failed to uphold these findings,[3–5] and now it is generally conceded that at least cortisone and hydrocortisone are not direct gastric stimulants. The corticords are, however, necessary for gastric secretion, shown by the fact that adrenalectomy is accompanied by a profound decrease in secretion which can be corrected by cortisone administration.[6] Other work demonstrating this "permissive" role[7] shows that cortisone will potentiate the secretagogue activity of methacholine (Mecholyl®),[8] histamine,[9] and gastrin.[10] As this work was done with the gastric pouch secreting at near physiological levels, the question arose concerning the effect of cortisone on the gastric output when the pouch is secreting under the effect of a large dose of secretogogue so that the secretory response is near maximum. Can even this secretion be increased by hydrocortisone, or would the corticoid cause a decrease?

The following experiment was carried out to examine this question and further, in the process of controlling the experiment, to repeat some of the previous controversial work in this field.

METHOD

Twenty-seven mongrel dogs with Heidenhain pouches were used for the experiment which is divided into 4 phases. It originally was planned that each dog would go through each phase, but this proved unnecessary. The first phase was to determine whether the pouch output varied with the time of day, the second, to see the effect of hydrocortisone by itself on the pouch secretion, the third, to ascertain if the time of day influenced the pouch response to histamine in beeswax, and the fourth, to judge the effect of hydrocortisone on the histamine-induced hypersecretion. For these experiments histamine phosphate was used throughout, which yields 360 mg. of histamine base per gram of whole compound. It was combined with mineral oil and beeswax after the method of Hay and associates.[11]

Each animal was deprived of food the night before and water at 6:00 A.M. the day of the test. A collecting balloon was attached to the pouch cannula at 8:00 A.M. and emptied every hour to get 8 one-hour specimens, the animal taking neither food nor water during this day. This consituted phase 1 and was done on 15 of the dogs. Phase 2 was identical except that 100 mg. of hydrocortisone was injected intravenously after the third hourly specimen was obtained. This was done on 12 dogs. Phase 3 was again the same as phase 1, except that 30 mg. of histamine base in beeswax was injected intramuscularly at 7:00 A.M., allowing an hour for the full secretory action to begin. Phase 4 was the same as phase 3 except that 100 mg. of hydrocortisone was injected intravenously after the third hourly collection was obtained.

RESULTS

Phase 1 was done on only 15 dogs as it became obvious that there was no significant variation in pouch secretions occurring during the test day.

Phase 2 was done on 12 of the dogs as again it became apparent that there was no increase in pouch secretion after the injection of hydrocortisone. The average hourly secretion of total acid was 0.0034 mEq. for the three hours before hydrocortisone and 0.0022 mEq. hourly secretion for the five hours after hydrocortisone.

The results of phase 3 (histamine alone) are listed in the table. As stated above, this phase was done to see if the response to histamine in beeswax varied with the number of hours from the injection. More specifically, since in phase 4 the hydrocortisone was injected between the

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TABLE

THE RESULTS OF HYDROCORTISONE ADMINISTRATION ON THE HISTAMINE-STIMULATED POUCH

Hourly gastric secretory responses to 30 mg. of histamine base in beeswax alone and to histamine in beeswax followed by hydrocortisone given at the third hour. Under the number of each animal the mEq. collected per hour is shown in column form.

Each animal, where possible, was tested in both phases and in some instances, however, only 1 type of examination was done accounting for the empty columns in the table. The average hourly output for first three hours, using histamine alone, of all 42 runs is 0.149 mEq. of acid while for the next five hours it is 0.145 mEq., showing that the histamine-induced secretion does not vary significantly with the time of day. The average hourly output for the first period in the histamine plus hydrocortisone group is 0.131 mEq., while for the second period it is 0.138 mEq., an insignificant difference.

Dog No.	*11*	*12*	*14*	*15*			*16*		*17*	*19*	*24*		*28*	
Histamine only	.452*	.234	.174							.645			.234	.044
	.442	.288	.150							.532			.355	.016
	.47	.27	.085							.543			.355	.121
	.498	.27	.102							.542			.316	.106
	.415	.264	.186							.254			.314	.11
	.455	.298	.131							.151			.329	.151
	.69	.348	.128							.022			.126	.083
	.49	.292	.131							.036			.176	.035
		.262		.039	.008	.075	.26	.036	.39		.009	.146		
		.337		.069	.015	.085	.246	.021	.47		.025	.143		
		.297		.125	.018		.238	.01	.47		.063			
Histamine plus hydrocortisone		.372		.113	.125	.104	.302	.042	.52		.094	.172		
		.28		.050	.139	.094	.370	.04	.65		.162	.161		
		.288		.088	.155	.127	.315	.02	.43		.119	.103		
		.288		.081	.057	.085	.253	.03	.32		.146	.058		
		.350		.048	.016		.30	.04	.4		.145			

Dog No.	*29*		*30*		*32*	*34*	*35*	*76-B*	*76-E*			*79*		*79-B*	
Histamine only	.241	.028	.008	.081	.018	.045	.006	.219	.251	.234	.260	.042	.016	.076	.046
	.324	.185	.223	.12	.003	.134	.002	.215	.260	.217	.225	.026	.014	.088	.039
	.294	.114	.175	.183	.108	.336	.011	.182	.226	.267	.181	.025	.013	.069	.033
	.261	.151	.152	.156	.028	.348	.10	.07	.192	.221	.257	.036	.01	.075	.027
	.23	.074	.085	.168	.053	.302	.09	.302	.163	.195	.223	.041	.019	.064	.044
	.186	.079	.149	.147	.053	.403	.223	.050	.142	.267	.182	.024	.024	.047	.037
	.172	.105	.063	.215	.036	.339	.224	.247	.147	.272	.229	.035	.009	.073	.036
	.322	.125	.128	.134	.026	.258	.134	.136	.093	.165	.180	.037	.031	.055	.053
			.108		.038	.398	.164	.002	.113	.078	.324	.026	.040	.047	
			.176		.034	.389	.103	.089	.093	.110	.333	.017	.037	.056	
			.142					.102	.094	.118	.388	.019	.033	.068	
Histamine plus hydrocortisone			.085		.101	.434	.209	.169	.13	.159	.360	.049	.050	.084	
			.147		.051	.316	.084	.074	.103	.168	.395	.058	.033	.068	
			.054		.063	.327	.115	.077	.092	.074	.273	.037	.031	.031	
			.012		.039	.264	.08	.077	.054	.151	.260	.010	.020	.072	
			.039					.063	.123			.020	.025		

*Milliequivalents of hydrochloride

Dog No.	80		81		82		83			84		84-C			
Histamine only					.029*	.059	.139	.047	.010	.148	.163	.031	.049	.036	.097
					.033	.017	.011	.045	.007	.225	.157	.024	.057	.029	.108
					.056	.072	.136	.048	.032	.085	.085	.056	.085	.046	.129
					.055	.045	.175	.047	.043	.171	.125	.093	.077	.052	.076
					.013	.045	.025	.049	.037	.231	.145	.071	.110	.024	.132
					.015	.052	.163	.050	.048	.215	.158	.087	.060	.043	.095
					.01	.053	.036	.037	.040	.214	.161	.068	.059	.078	.026
					.09	.041	.208	.032	.024	.193	.172	.060	.114	.103	.109
	.047	.026	.152	.205	.038	.019	.126	.01	.05	.114	.099	.087			
	.044	.024	.235	.280	.042	.018	.086	.031	.035	.087	.064	.126			
	.044	.014	.261	.261	.036	.010	.127	.026	.029	.220	.155	.150			
Histamine plus hydrocortisone	.041	.014	.020	.418	.027	.036	.091	.026	.018	.203	.174	.170			
	.066	.013	.05	.374	.031	.021	.09	.028	.036	.205	.129	.114			
	.044	.012	.171	.306	.001	.033	.112	.020	.023	.126	.212	.108			
	.038	.015	.193	.272	.025	.012	.104	.017	.037	.207	.169	.064			
	.068	.017	.096	.175	.03	.047	.095	.012	.010	.089	.164	.096			

Dog No.	86		86-B				88-C		
	.121	.201	.114	.160	.329	.508	.113	.117	.21
	.115	.210	.041	.054	.377	.458	.320	.210	.049
	.125	.145	.101	.104	.290	.301	.113	.153	.044
Histamine only	.107	.131	.386	.166	.404	.391	.186	.062	.09
	.097	.104	.286	.074	.389	.350	.137	.182	.118
	.050	.085	.331	.065	.358	.441	.106	.108	.158
	.075	.105	.253	.082	.290	.294	.165	.123	.136
	.068	.099	.039	.015	.223	.330	.107	.143	.095
	.229		.312						
	.098		.319						
	.172		.272						
	.131		.356						
Histamine plus hydrocortisone	.115		.314						
	.139		.270						
	.117		.355						
	.119		.154						

*Milliequivalents of hydrochloride

third and fourth hour and phase three was its control, we wished to know if the secretory response in the first three collection hours differed from the response in the last five collection hours. Obtaining the hourly output for these 2 time periods showed that an average of 0.149 mEq. of total acid was secreted per hour in the second five hours—an insignificant difference.

The results of phase 4 (histamine plus hydrocortisone) are also detailed in the table, and here the dashed line between the third and fourth hours indicates the time of injection of 100 mg. of hydrocortisone intravenously. Again the average hourly output for the first three hours was compared to the hourly output of the succeeding five hours. This was 0.131 mEq. per hour for the first period and 0.138 mEq. for the second, again showing no significant difference.

DISCUSSION

The interaction between histamine and hydrocortisone, being basic to this work, was explored first. The pituitary-adrenal mechanism inhibits the release of histamine and both pituitary and adrenal extracts exert this action,[12] presumably, through the potentiation of histaminase by the adrenal products.[13] This, however, is seen only in certain tissues as, at least in the rat, the concentration of histamine in the stomach is increased by corticoid administration, possibly explaining the ease of production of cortisone ulcer in this animal.[14] Cortisone exerts a protective effect against histamine shock in the adrenalectomized animal[15] but confers only slight protection in the intact animal, and then only in very large doses.[16] Thus, there is evidence of a physiological, but not a chemical, antagonism between these drugs. In the doses used in this work all physiological effects are considered to be overpowered.

The number of acid determinations listed here may well appear to be excessive but the extreme difficulty of standardizing these experiments leads us to believe that only with repeated determination and many samples will enough randomicity enter to yield reasonably reliable results. Evidence for this is readily observed in the table where the acids obtained are seen to vary within wide limits. Even when the same animal was tested in the same way on different days the acid levels varied widely.

The output of a Heidenhain pouch is quite constant but extremely small during a fasting eight-hour period, and it is not influenced by 100 mg. of hydrocortisone. Shay[8] noted an increase in acid production occurring about the sixth hour, but Ragins[4] did not find an increase. Histamine in beeswax exerts a very uniform secretory activity over the collection period which again is not influenced by hydrocortisone. The reason for this lack of influence is not felt to be due to a chemical antagonism between the drugs as mentioned above but may result from the pouch secreting at a maximum rate. Unfortunately, these pouches were not tested to determine their maximum secretory rate so this is only conjective.

The role of the corticoids in gastric secretion appears, at this writing, to be best described as "permissive." If corticoids are not present, the stomach cannot secrete; but as they are available in larger quantities the stomach responds in greater degree to such stimulants as mecholyl and gastrin. The stomach responds this way to histamine when smaller doses are used than those given for this study.

Cortisone has the further property of homeostasis or influencing a reaction to remain within a certain physiological range. Can the fact that it does not decrease the histamine hypersecretion be interpreted as indicating no such homeostatic action on the stomach, or is this mechanism so geared as to react maximally to a food stimulus and then be suppressed by other mechanisms such as the antrum?

SUMMARY

A study was carried out on Heidenhain pouch dogs to determine the effect of hydrocortisone on basal gastric secretion and histamine-induced hypersecretion. Hydrocortisone does not affect histamine hypersecretion, nor does it act as a gastric secretagogue.

The author wishes to express his appreciation to Mrs. Mildred Lee for the preparation and typing of this manuscript.

This work was done under the auspices of the Veteran's Administration.

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IDENTIFICATION OF LYMPH NODES dissected in pelvic and abdominal surgery is facilitated by placement of nodes in proper position on a board containing a mock-up of major arterial vessels. The board is sent to the pathologist and returned with his report, which accurately determines appropriate radical or palliative procedure.

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Maintaining identity of excised lymph nodes. Mayo Clin. Proc. 39:273-274, 1964.

MAMMOGRAPHY is not effective as a routine screening procedure for preclinical carcinoma in asymptomatic premenopausal women older than 40 years. The technique is of definite value, however, for examination of patients with breast symptoms or breast abnormality found by physical examination and for those who have had mastectomy for cancer. Routine mammography also may be useful for diagnosis in asymptomatic postmenopausal women, although the detection rate is low. Several possible reasons may account for the low diagnostic yield of routine mammography: Small carcinomas are difficult to identify as malignant tumors, both large and small carcinomas may be obscured by the radiologically dense breast parenchyma common in premenopausal and menopausal women, and patients may be highly selected. Mammographic diagnosis is possible in only about 85% of palpable tumors that usually are much larger than the lesions looked for in routine screening. Mammography of 5,014 women 40 years of age or older without significant breast symptoms or signs revealed only 8 carcinomas, all in postmenopausal women. Tumors were invasive, scirrhous adenocarcinomas that had not spread to axillary lymph nodes. The breast parenchyma was atrophic and the lesion was clearly outlined against the fatty background in each case.

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Mammography as a routine screening examination for detecting breast cancer. Amer. J. Roentgenol. 92:14-20, 1964.

Disorders of Speech and Language

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SPEECH DISORDERS may exist either [1] on the basis of interfering lesions of the organs of speech and the immediate innervation of these organs with consequent disturbances in phonation and articulation or [2] on the basis of hemispheric lesions with disruption of the central mechanisms of the language process with resultant aphasia.

ARTICULATION

Articulation refers to the proper enunciation of words or sentences. Articulation requires the coordinated movement of the lips, palate, tongue, and cheeks, all coordinated with the function of the vocal cords. Hence, articulation requires the coordinated action of the fifth, seventh, ninth, tenth, and twelfth cranial nerves. A disturbance of articulation on an organic basis is referred to as *dysarthria*. A disorder of function of the larynx produces disturbances of phonation (pitch, intensity, and quality of sound) and is referred to as *dysphonia* or *aphonia*. A disturbance of articulation with no organic basis but due to involvement of the peripheral articulatory mechanism is called *dyslalia*.

Normal articulation is dependent upon many factors ranging from proper neuromuscular control of the organs of articulation to proper cerebral synthesis and correlation. Hence, articulatory disturbances can arise from a wide range of neurological disturbances, each having its own characteristics.

DYSARTHRIA

Nuclear involvement (bulbar speech). Any lesion of the neuromuscular control of the muscles of articulation produces dysarthria. Such involvements implicate the cranial nerves or the brainstem nuclei. The character of the dysarthria will be determined by the cranial nerves or nuclei which are involved.

1. *Fifth cranial nerve.* Unilateral involvement produces no speech disturbance. Bilateral involvement produces typical bulbar speech. The most common causes of this type of dysarthria are tetanus and occasional cases of poliomyelitis.

2. *Seventh cranial nerve or nucleus.* Such a defect results in an inability to pronounce labials and dentolabials such as "P," "B," "F," and "V." The speech becomes slurred. This type of speech disturbance is encountered chiefly in bilateral facial involvement such as is seen in Guillain-Barré's syndrome, myasthenia gravis, and the myopathies. It may occur in severe, unilateral Bell's palsy because of the inability to close the mouth or distend the cheeks.

3. *Ninth cranial nerve or nuclei.* Involvement results in paralyses of the soft palate with an inability to close off the nasal cavity from the mouth. This results in an inability to pronounce volar sounds such as "N," "M," and "NG." The speech becomes nasal. This nasal quality is increased in stooping forward and may disappear when the patient is in bed, since the palate drops backward in place. A nasal speech is often encountered in postdiphtheritic paralysis and in poliomyelitis.

4. *Twelfth cranial nerve or nuclei.* Involvement produces weakness of the tongue with an inability to pronounce linguodentals— "TH," "S," and "Z"—and linguopalatals—"SH," "T," "L," "D," and "R." The speech is indistinct or lisping. Diseases such as amyotrophic lateral sclerosis and superior bulbar palsy manifest this form of dysarthria.

5. *Combined cranial nerve or nuclear involvement.* Extensive cranial nerve palsies produce impaired articulation, phonation, and swallowing. The speech is muffled or guttural and the patient speaks as if his mouth were full.

6. *Upper motor neuron speech (pseudobulbar speech).* The articulatory muscles on each side

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are innervated by both cerebral hemispheres. Hence, a unilateral cerebral lesion does not produce dysarthria. However, if the motor system of both sides of the brain is involved, a dysarthria will appear which is identical with a bulbar involvement and has been called pseudobulbar speech. This type of dysarthria is often associated with difficulty in swallowing, mental changes, and uncontrolled emotionality. It is seen in a number of conditions such as congenital diplegia, vascular lesions of both hemispheres, inflammatory lesions, and diffuse degenerative lesions.

Cerebellar dysarthria. Coordination of articulation suffers when the cerebellum is involved, resulting in disturbances of speech. The speech may be slow and stumbling with an explosive quality often referred to as a staccato speech, or it may be jerky and syllabic with each component syllable of the word being pronounced deliberately and slowly as if it were a separate word. This is the scanning speech resembling the scanning of poetry. Cerebellar dysarthria is encountered in multiple sclerosis and Friedreich's ataxia.

Cerebral dysarthria. The speech is hurried, careless, and clumsy with the omission of letters, syllables, and phrases and the running together of words. This is the typical slurred speech. This type of speech disturbance is seen in general paresis, alcoholism, intoxications, and diffuse brain damage.

Extrapyramidal dysarthria. The speech may be slow, labored, intermittent, and jerky. The patient often talks in a monotone and lacks modulation of the voice, often talking in a whisper. This is referred to as a monotonous speech. The speech may be hesitant, with sudden outpouring of rapid speech. This is called a festinant or explosive speech. The above types of dysarthria are seen in parkinsonism.

In chorea the speech is jerky, irregular, and hesitant, while in athetosis the speech has a jerky, groaning characteristic due to spasmodic contraction of the tongue and the pharynx.

Psychogenic dysarthria. In agitated individuals the speech is broken and tremulous. In hysteria the speech varies from time to time. It is bizarre in nature and does not resemble any organic lesion. It often has an abrupt onset with only short periods of speech difficulty. Habit spasm produces a speech characterized by grunts, groans, and barking sounds. In depression the speech is slow, hesitant, and often associated with mutism. Stuttering is a faltering speech which is characterized by stumbling and hesitancy with habitual and spasmodic repetition of consonants or syllables and voluntary pauses.

Testing for dysarthria. Many test phrases can be used. The following have proved most useful and include chiefly labials and linguals (L, R, P, B, T, D): [1] third riding artillery brigade, [2] Methodist Episcopal, [3] newly laid linoleum, [4] truly rural, [5] Constantinople, [6] around the rugged rock the ragged rascal ran, [7] voluntary retributions, and [8] hippopotamus.

DYSPHONIA AND APHONIA

Phonation refers to the sounds produced by vocal cord function; pitch and intensity of the voice are largely determined by the vibration of the cords. *Dysphonia* occurs when one vocal cord is paralyzed (recurrent laryngeal branch of the tenth cranial nerve) or when a local process, such as tumor or inflammation, interferes with the normal vibration of the cords. The voice in dysphonia is hoarse. The most common cause is acute laryngitis.

Aphonia is the absence of voice. It is usually due to total bilateral interruption of vocal cord function from paralysis or laryngeal disease. An aphonic person can still speak but only in a whisper; he cannot cough forcibly when the cords are totally paralyzed. Hysterical aphonia is a special case.

DYSLALIA

This is an impaired articulation in the presence of an intact nervous system. It is caused by involvement of the peripheral articulatory mechanism. The most common causes of dyslalia are wounds of the lips, tongue, palate, and mouth; cleft palate; harelip; tumors of the tongue and palate; and edentulism.

APHASIA

Whereas disturbances of phonation and articulation imply interference usually at or peripheral to the cranial nerve nuclei, aphasia refers to disturbances in speech from involvement of the hemispheric mechanism. The earlier workers in aphasia tended to separate out "pure" defects in the language processes of individuals with hemispheric lesions and attempted to correlate them with very restricted cortical areas. Subsequent work has demonstrated the fallacies in such refinements beyond rather gross generalities.

Speech or language is a part of a complex function known as symbolic formulation and expression. This comprises not only speaking and comprehension of the written and printed word but also such achievements as poetry, song, painting, and so on. Symbolic thinking is perhaps the most striking mental achievement of man. In its most complex form, symbolic thinking and

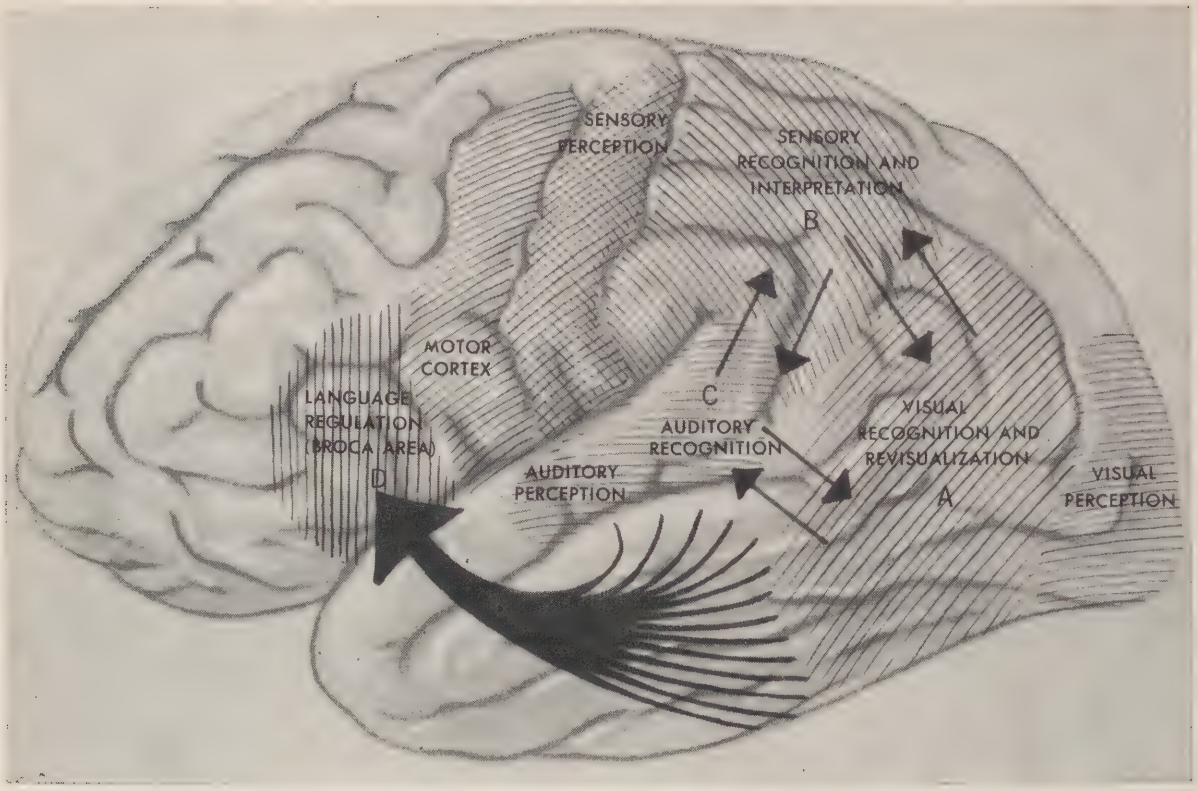


Fig. 1. Language formulation. Note the interplay between visual, auditory, and sensory areas.

expression is a function of the entire brain. The disintegration brought about by cerebral disease, however, shows that there is a degree of localization of certain of its components.

Language formulation (Fig. 1). Language is normally learned by ear, and comprehension precedes speech. Recurring sound patterns become associated with recurring experiences and assume identity and meaning. At the same time as the child is acquiring control of the mechanisms of speech through babbling and imitating, he is learning to show the responsiveness to others which is the basis of communication. Diverse and complex cerebral processes must mature and integrate before the first word appears.

At birth an infant can see, hear, and feel but these sensory perceptions have no meaning, being basic functions and similar in all infants. Within a short period of time, the child begins to form and store visual, auditory, and sensory memory patterns in that part of the brain adjacent to the primary sensory areas. These sensory memory patterns differ from infant to infant depending upon the experiences that play a role in producing such patterns. Hence, language function begins to differ in different individuals very early in life.

Soon the infant begins to make associations between objects seen and sounds and to form associations of such objects. Hence, there is now an interplay of associations developed between the visual, auditory, and sensory areas of the brain on the left side, or dominant hemisphere. Still later, as language function further develops, the infant or child is able to recall (revisualize) an object symbol without actually seeing the object. For example, the mother symbol can be recalled from the sound of her voice in another room or from the need of her comforts when the infant is hungry.

Neither reading nor writing can be learned successfully until language is well established. Reading consists of learning complex sets of visual patterns in association with auditory patterns previously learned and invested with meaning. Writing demands complex visual-motor coordinations as well. When the child begins to read and write, symbolic language is added. Since every word is associated with the object it represents—the sound it makes and the nature of the object—it is apparent that this symbolic area must be associated with the visual, auditory, and somatosensory areas of the brain.

While these basic language areas are being developed, they are naturally influenced by the surrounding cortex since daily experiences must

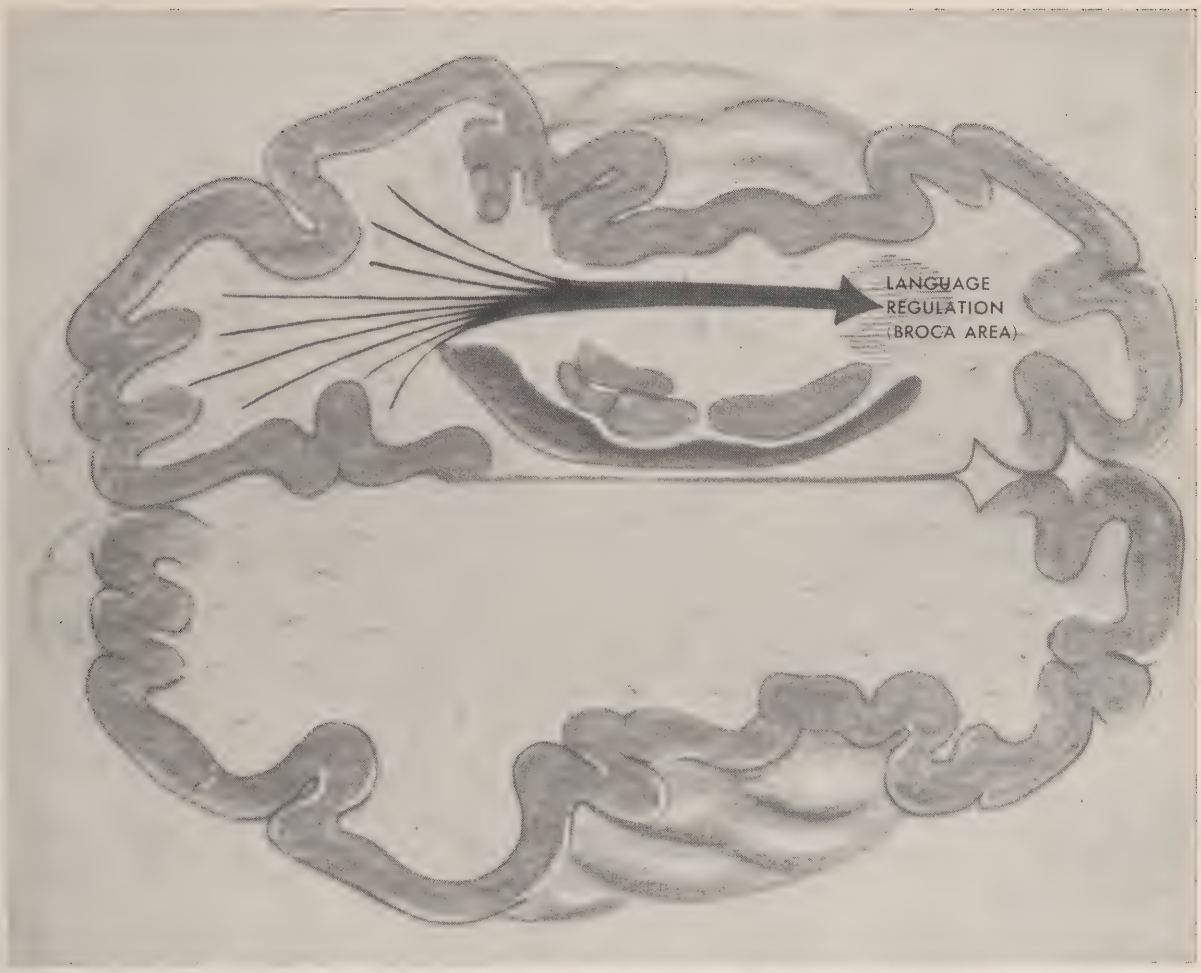


Fig. 2. Language expression. Formulated language must pass through the temporal isthmus to reach the motor areas of expression. Note its proximity to the internal capsule.

in some way color the various components of language. It is this interplay from the higher centers that really individualizes language and adds to it the emotional coloring that is so important.

The formulation of language is therefore primarily a sensory function and demands the integration of complex auditory, visual, and sensory events. It takes place in that part of the brain containing these sensory functions, namely, in the posterior half of the dominant hemisphere. Generally in language formulation, the basic auditory, visual, and sensory functions are integrated with experiences which give these patterns meaning and with emotional interactions which underlie communication.

Language expression (Fig. 2). Once language is formed, it must be expressed or communicated. Language expression is a motor function and must be carried out by the motor cortex regulating the muscles of articulation. These cells of the motor cortex, in order to properly articulate, must learn how to coordinate to form words. This regulation of motor function in speaking is carried out by the cortical area just anterior to the motor cortex in the region called Broca's area.

Since language is formulated in the posterior portion of the brain and expressed in the more anterior motor areas, the formulated language must be transmitted anteriorly to reach the motor areas of expression. To do so, these language systems must narrow down to a small tract as they pass through the temporal isthmus just lateral to the internal capsule. A small lesion in this area could, therefore, destroy all the speech functions and could result in complete loss of all expressive speech.

This temporal speech area receives its blood supply from one of the small striated branches of the middle cerebral artery and is frequently implicated in cerebrovascular disease. Involvement of this artery results in a right-sided motor weakness and an expressive speech defect.

Although language is an integrated function of much of the brain, the disintegrations brought about by cerebral disease indicate that there is a degree of localization of certain of its components. This is well demonstrated by the presenting types of speech disorders which can be used as a clinical classification. The 5 most commonly observed patterns are as follows:

1] Severe impairment of all language modalities. Patients in this group are severely impaired in understanding language and have no functional speech, reading, or writing. Prognosis is poor.

2] Impairment of auditory retention span and auditory recall. Patients in this group understand short language units but lose the meaning easily in connected discourse because of reduced auditory retention span. They mispronounce words because auditory recall is defective. They have trouble recalling words and using the structural forms of language. Reading and writing reflect the defects found in speech. Simultaneous improvement occurs in all language modalities, and the prognosis for this group is excellent.

3] Impairment of auditory processes with coexisting visual involvement. Patients in this group are like those in the group above but in addition have specific difficulty recognizing and recalling written and printed symbols. Hemianopsia is always present, but this is not diagnostic in itself. Spatial disorientation is sometimes but not always present. The prognosis for recovery of speech is good, but recovery of reading and writing ability is slower and more difficult.

4] Impairment of auditory processes with coexisting sensorimotor involvement. In addition to the basic language deficit described above, patients in this group have difficulty coordinating and controlling the neuromuscular mechanisms of speech. However, articulation problems are usually less significant than the auditory ones and respond more readily to treatment. Thus, the patient usually learns to repeat long before he has acquired the vocabulary and structural forms of language needed for communication. Prognosis is limited recovery.

5] Scattered auditory, visual, and motor involvement, compatible with generalized brain damage. Patients in this group have commonly retained a good deal of language, in one modality or another. However, they do not respond well to treatment because of unstable physiological, neurological, and psychological conditions. They are usually incapable of sustained or self-directed effort. Emotional lability is frequently present. Prognosis is necessarily guarded.

From a practical point of view one can list some clinical guides to language problems based upon the above discussion:

1] Language formulation is primarily the function of the posterior half of the left cerebral hemisphere. Lesions in the anterior half of the brain, or in the right hemisphere, produce no language difficulties.

2] A lesion of the parietotemporo-occipital region rarely produces a complete language loss because of the extensiveness of the speech formulation areas. In lesions of this area, the prognosis for recovery of some speech functions is good.

3] Complete loss of motor speech in the presence of good comprehension suggests a lesion in the temporal isthmus and is usually associated with a hemiparesis.

4] The younger the patient, the better the prognosis for recovery of language function.

5] Because of the many different components of language, language impairment rarely appears as an isolated involvement of any single component such as vision or hearing but usually shows involvement of many functions in some degree.

INTRAVENOUS INJECTION OF EPINEPHRINE and norepinephrine inhibits gastric secretion in dogs with Heidenhain pouches, apparently as an indirect result of decreased gastric mucosal blood flow. Although total gastric blood flow shows variable alterations, mucosal flow is consistently depressed, suggesting the possibility of opened arteriovenous shunts. Mucosal flow is reduced more by epinephrine than by norepinephrine, and doses greater than 0.25 μg. per kilogram per minute do not enhance the effect.

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Dangers of Retrograde Percutaneous Angiography for Visualizing Extracranial Vessels

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THE CURRENT INTEREST in surgery of the extracranial vessels (internal carotid and vertebral artery systems) has dramatically increased the number of procedures directed toward visualizing these vessels. The complications of direct visualization of the carotid and vertebral artery systems by injection of the dye through a needle placed directly into the artery are well known. Therefore, the purpose of this paper is to call attention to the potential hazards of arteriography directed toward visualization of these vessels by instillation of the contrast media distant from the vessel to be visualized and by injecting the dye through a catheter into the brachial artery, the femoral artery, or via the subclavian approach. The hazards of catheterization techniques of visualizing the extracranial vessels need emphasizing, and the cases selected for such arteriography deserve careful selection in order to avoid throwing these worthwhile procedures into disrepute. Recently 2 patients subjected to retrograde percutaneous arteriography developed major complications. A discussion of these cases serves to underline the problems connected with these techniques.

CASE HISTORIES

Case 1. Ten days before admission to the hospital, a 63-year-old woman had an onset of either blindness or blurring of vision in the left eye, transient in nature. On the date of admission, she awakened with a severe headache and tinnitus and then suddenly developed a dysarthria with some paresthesias of the hands. The dysarthria was marked and the patient's speech was almost unintelligible. There was a previous history of borderline diabetes and hypertension for ten years, with pressures ranging from 190 to 220 over 90 to 120. The systolic blood pressure was 220/120. The patient had a prominent bruit over the left carotid vessels and, to a lesser extent, a bruit over the right carotid vessels. Coincident with the insertion of the femoral catheter before retrograde angiography, she developed a shock-like picture.

At the time the patient was initially examined, the dysarthria was marked. There was a right lower facial lag. The patient was oriented. The blood pressure was fluctuating and continuous intravenous metaraminol (Aramine®) was required to maintain her blood pressure. The decision was made to discontinue the angiographic procedure. The patient continued to require the use of intravenous Aramine®. Serial electrocardiograms established the diagnosis of a myocardial infarction. The patient succumbed on the eleventh hospital day from myocardial infarction. Consent for autopsy could not be obtained.

Comment. The patient, as a complication of femoral artery catheterization, developed a drop in blood pressure complicated by the development of a myocardial infarction.

Case 2. When this 60-year-old man was seen initially, he complained of incoordination involving the left arm, headaches, sensation, for past two years, of his feet being asleep, and a balance difficulty for which he used a cane. Two years before his initial examination, on awakening in the morning, he found he was unable to move his left lower extremity. At that time he was found to have a flaccid paralysis of the left lower extremity with a marked ataxia involving the left upper extremity. This episode lasted about an hour and was associated with marked nystagmus on looking to the left. There was a decrease in alternate motion rate of both hands and in-

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creased reflexes and marked clonus in the right lower extremity, but no Babinski. There was also considerable weakness in the lower right extremity and decrease in finer touch in the left upper extremity. The patient at that time was admitted to a hospital for investigation and developed an episode associated with paralysis of all 4 extremities. There were bilateral ankle clonus and increased reflexes in both lower extremities. At the time the patient was discharged, he had gradually improved but continued to have a definite weakness and ataxia in the left upper extremity and seemed definitely ataxic in both lower extremities as well.

The initial examination was recorded as follows: "The cranial nerves are negative. The systolic blood pressure is 160 and the diastolic 100. The patient has some involvement of the finger-to-nose on the left and adiadokokinesis on the left. Although he complains of sensory disturbance involving the left hand, it is not demonstrable. The patient has a marked ataxia with involvement of the heel-to-knee-to-toe test on the right. There is spasticity and weakness involving the right lower extremity. The biceps and triceps reflexes are active and equal bilaterally. The right knee and right ankle jerks are greater than those on the left, and there is sustained ankle clonus on the right. The toe signs are negative. The abdominal reflexes and cremasteric reflexes can be elicited. The sensory examination is negative."

The patient was hospitalized for further investigation. Bilateral brachial angiography was performed with visualization of the vertebral arteries which were within normal limits. In the course of the examination, the X-rays suggested a relative coarctation or interruption in the course of innominate artery and a study of the arch of the aorta was recommended. A catheter was inserted via the femoral artery and the aortogram proved to be within normal limits. Subsequently bilateral carotid angiography was carried out, and complete occlusion of the left internal carotid artery at its origin was demonstrated. Ten days following the angiographic procedures, the patient developed 2 bouts of pulmonary embolism with a typical clinical picture of chest pain and shock plus hemoptysis. He responded to the use of anticoagulant therapy and oxygen. The patient was stabilized on anticoagulant therapy and discharged.

Comment. The patient developed pulmonary embolism as a complication of his retrograde percutaneous angiography. The site of this embolism probably was venous in origin and due to an injury of one of the veins which was probably inadvertently punctured or damaged during the catheterization procedures.

Discussion. The complications of retrograde percutaneous arteriography may be divided into 2 groups: the minor complications and the major complications. With respect to the minor complications, these result in transient discomfort to the patient but lack late sequelae. These include (1) transient arterial spasm, (2) asymptomatic local hematomas, (3) relatively asymptomatic intramural or subintimal dye injections, and (4) relatively asymptomatic perforation of large vessels. The major complications include (1) arterial thrombosis, (2) arterial embolism, (With respect to the embolic phenomena, these are further subclassified into early embolic phenomena due to dislodgement of arteriosclerotic plaques and atheromatous material by the catheter or guide wire. The late embolic phenomena are usually the result of damage to the intima with formation of the thrombi along the torn intima and resulting embolization from these areas), (3) perforation of major vessels with serious complications, (4) renal complications, (5) bowel ileus and necrosis, (6) breaking off of the tip of the guide wire or catheter, (7) pulmonary embolism, (8) myocardial infarction subsequent to a drop in blood pressure at the time of the insertion of the catheter, and (9) reaction to the dye resulting in anuria or oliguria.

Lange,[1] in an excellent review of the complications of retrograde percutaneous angiography, reported that in a series of 11,402 procedures, a complication rate of about 3.7% was encountered. Of these, he estimated that 3% were minor complications and 0.7% were major complications with a mortality rate of .06%. In his series, 7 fatal complications were encountered. Lange reported a case of pulmonary embolism due to injury of the saphenous vein at the time of the catheterization procedure. Case 2, as reported above, probably falls into this group. In Lange's series, there was no instance of myocardial infarction following a drop in blood pressure at the time the catheter was inserted. Case 1, as reported above, adds this major complication to the literature.

CONCLUSION

Visualization of the extracranial vessels is not an innocuous procedure. Close collaboration between the physicians involved is mandatory if proper cases are to be selected. Having made the decision to proceed with the arteriography, every effort should be made to avoid complications. The major complications can be reduced by avoiding performance of the procedures on poor-risk patients. Low output failure, poor vascular

fitness, and arteriosclerotic conditions are determining predisposing factors in the production of major complications. With respect to the minor complications, these can be reduced by meticulous attention to details by the experienced operator and immediate postoperative care.

Two patients are presented who developed major complications following angiography. One succumbed to a myocardial infarction, which occurred following a drop in blood pressure at the time of the insertion of the catheter. The other developed pulmonary embolism, probably as a result of injury to a vein which was probably punctured or damaged during the catheterization procedures.

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CHLORPROPAMIDE (Diabinese®) in daily oral doses of 250 to 375 mg. controls hyperglycemia adequately in most diabetic patients with very little risk of hepatic dysfunction. Patients requiring 500 mg. or more, however, probably should be transferred to insulin therapy. Serum transaminase and alkaline phosphatase determinations are the most reliable tests of hepatic function and should be performed regularly. The cephalin flocculation test, on the other hand, is nonspecific and may be misleading, since chlorpropamide-treated patients often have positive tests without corresponding alterations in serum proteins or other liver function parameters. An average daily dose of 240 mg. of Diabinese® administered to 181 diabetic patients for one week to fifty-seven months gave good to excellent control in 84.6% and fair in 4.4%. Although the incidence of positive cephalin flocculation tests was significantly increased, the only other abnormalities in liver function detected were minor alterations in the chemical and electrophoretic pattern of gamma globulins.

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DIFFERETIATION between cirrhosis and obstructive jaundice is aided by determination of retained sulfobromophthalein sodium (Bromsulphalein®) and identification of conjugates after a single injection. In patients with cirrhosis, retention declines faster and percentage of conjugates in serum is significantly less than with obstructive jaundice. The technique does not distinguish between intra- and extrahepatic obstruction. However, such parameters are diminished in most hepatobiliary diseases, indicating function disturbance at cellular and subcellular levels after extrahepatic bile duct obstruction. With continuous infusion, percentage of conjugates is related to time as well as liver function. Rate of appearance is highest in patients with extrahepatic obstruction, suggesting substantial reflux from liver to blood. Data are based on metabolism and transport of Bromsulphalein® studies in 33 patients with hepatic disease and 19 controls.

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Left Atrial Myxoma and Fatal Abacterial Pneumonia

Report of a Case

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Previous studies[1,2] have alluded to the importance of preexisting cardiovascular disease in the pathogenesis of fatal abacterial pneumonia. The most commonly reported underlying disorder has been rheumatic heart disease.[3] It is the purpose of this report to present what we believe is the first case of left atrial myxoma complicated by an overwhelming pneumonia of viral origin.

CASE REPORT

A 23-year-old male was admitted to the United States Army Hospital at Nürnberg, Germany, with the recent onset of dyspnea and pleuritic chest pain. The patient was well until two weeks before admission when he developed a dry, hacking cough. Two days before admission he began coughing up blood-tinged sputum. On the day before admission symptoms of chills, anterior midline pleuritic chest pain, and dyspnea on exertion appeared. He was admitted to the hospital the following morning in acute respiratory distress. There was no past history of scarlet fever, acute rheumatice fever, or respiratory or cardiac disease. At age 16 a heart murmur was noted during a routine examination. This murmur was not recorded on induction medical examination. He denied any decrease in exercise tolerance. Two weeks before admission he had minor dental work performed. There was no history of exposure to pscittacine birds, toxic fumes, or wild animals. There was no history of syncope or palpitation. The patient had had close contact with a German Shepherd dog which was destroyed one day previously by a veterinarian for early distemper. Postmortem examination of the dog was not performed. There was no known family history of chronic respiratory or cardiac disease.

On physical examination the patient was thin, well developed, and perspiring profusely. He was dyspneic at rest and orthopneic. Cyanosis was apparent. Respirations were 44 per minute and regular. The blood pressure was 122 per 75 mm. Hg, the pulse 104 per minute, and the oral temperature 99° F. The neck veins were distended when the patient was lowered to 30°. There was no scleral icterus, conjunctival injection, or lymphadenopathy. The trachea was in the midline. The chest was resonant to percussion but bilateral moist rales were heard diffusely throughout both lungs. There were no physical findings of cardiac enlargement. A soft and short, decrescendo, medium-pitched, systolic, apical murmur radiating to the anterior axilla was audible. The patient was in the sitting position during auscultation. The second sound in the pulmonic area was increased in intensity but audible splitting was not present. The liver was not enlarged and peripheral edema was not present. There were no other pertinent findings.

Chest X-ray (Fig. 1) revealed diffuse perihilar and radiating infiltrates involving all lobes of the lungs. The X-ray suggested pulmonary edema, uremic pneumonitis, or extensive bilateral interstitial pneumonitis. The heart was normal in size and configuration and no calcifications were seen in the heart shadow. Electrocardiogram showed sinus tachycardia, left deviation of the electrical axis, and an RR in lead VI. The arm to tongue circulation time (Decholin), in the supine position, was twelve seconds. The white blood cell count was 29,400 per cu. mm. with

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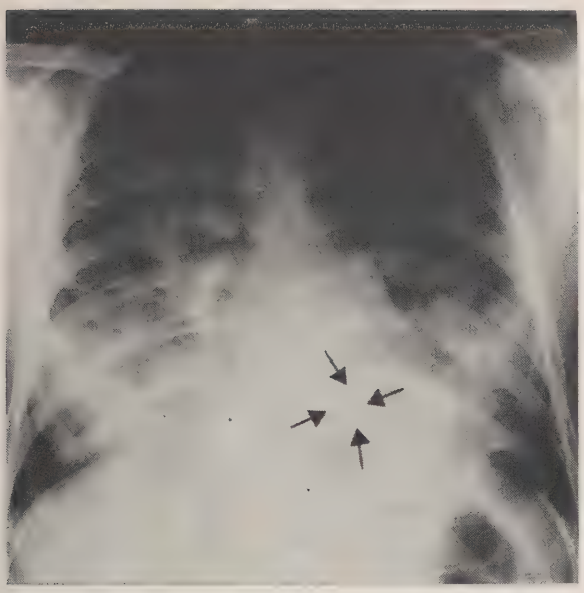


Fig. 1. Chest X-ray showing bilateral pulmonary infiltration and normal cardiac silhouette. The arrows note the position of the calcified tumor mass as determined by postmortem examination.

a predominant neutrophilia. The hemoglobin was 15.2 gm. per 100 ml., and the hematocrit was 47%. The erythrocyte sedimentation rate was 23 mm. per hour by the Wintrobe method. Urinalysis was normal and the BUN was 26.5 mg. percent. The sputum was tenacious, mucoid, and blood-tinged. On microscopic examination scattered gram positive cocci with rare pus cells were seen. Bacterial culture of the sputum demonstrated only Alpha streptococcus and Neisseria catarrhalis. A blood culture done on admission subsequently showed no growth after ten days incubation.

The prodromal symptoms of cough and chills, the admission chest X-ray and examination noting a normal sized heart, the normal circulation time, and the absence of previous cardiac symptoms were in keeping with a primary pulmonary disorder. A presumptive diagnosis of bilateral pneumonia of viral origin was made. The patient was treated with vaporized oxygen, fluids, and small doses of morphine sulfate for anxiety and restlessness. The patient showed initial improvement with less cyanosis and restlessness. This improvement was only temporary. His respiratory rate increased to 60 per minute and his temperature rose to 101° F. rectally. Less than six hours after admission the patient suddenly expelled a large amount of thick bloody material through his mouth and nostrils and his respiration ceased.

The principal findings at autopsy were confined to the cardiovascular and respiratory symptoms. Bilateral hydrothorax of 1,500 cc. and hydropericardium of 75 cc. were evident. The heart weighed 400 gm. The right ventricle was dilated. A 2 cm. square area of epicardial fibrosis was noted at the midposterior left ventricle overlying an area of transmural myocardial fibrosis. The coronary vessels were patent. The left atrial and ventricular musculature were hypertrophied. All valves except the mitral valve were normal. The leaflets and chorda tendinae of the latter were thickened and sclerotic as was the left atrial endocardium. A large, pedunculated, yellow, firm, partially calcified tumor mass arose at the base of the medial mitral leaflet partially occluding the annulus (Fig. 2). The tumor measured $3.2 \times 2.3 \times 2.0$ cm. On microscopic examination it was composed of stellate cells enmeshed in a stroma rich in acid mucopolysaccharides (Fig. 3) with areas of calcification and surface fibrin deposit. No evidence of rheumatic heart disease was observed. Evidence of coronary artery tumor embolization, recent or remote, was not encountered.

The lungs were large, heavy and boggy; the left weighed 1,225 grams, the right 1,475 grams. On cut section they presented an edematous and severely congested appearance. Numerous intimal atheromata were noted within pulmonary arteries. On microscopic examination, in addition to edema and congestion, areas of bilateral acute interstitial pneumonitis, with hyaline membrane



Fig. 2. Gross photograph of polypoid intra-atrial myxoma arising from the interatrial septum at the base of the medial mitral leaflet. The sclerotic valve may be seen inferior to the base of the tumor.

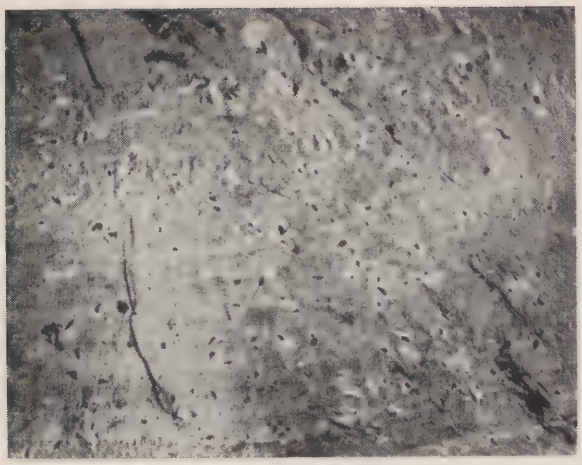


Fig. 3. The intra-atrial tumor shows numerous stellate cells in a homogenous myxoid stroma. An area of calcification is seen in the upper part of the photomicrograph. Hematoxylin and eosin, × 100

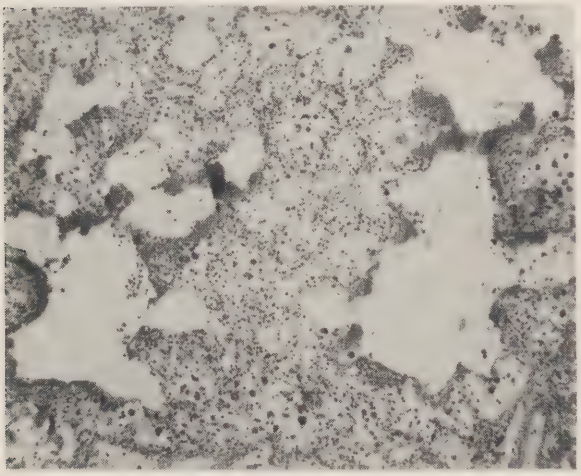


Fig. 4. Photomicrograph of lung showing a characteristic acute interstitial pneumonitis with prominent hyaline membrane formation. Hematoxylin and eosin, × 100

formation, were diffusely present and easily identified (Fig. 4). An accompanying acute, nonulcerative, tracheobronchitis was present. Hemosiderosis of the lungs was confirmed by iron stain. There was no evidence of medial hypertrophy of pulmonary vessels although scattered intimal atheromata were identified in various arteries. An intensive search for inclusion bodies, utilizing Lendrum Schorr's and Feulgen stains, was unsuccessful. Other findings included congestion of all viscera; evidence of mild, chronic, nonspecific jejunitis; and chronic prostatitis.

Postmortem cultures of blood and lung were sterile. An attempt at virus isolation from both lungs was unsuccessful although, during passage through monkey kidney, a suspected virus particle was discovered but subsequently lost on further passage.

DISCUSSION

The rapidly progressive downhill course in our patient was reminiscent of the description of fatal influenzal pneumonia in patients with rheumatic heart disease described by Louria and associates.[3] These authors noted that their patients entered the hospital within thirty-six hours after the onset of a typical influenzal-like illness with fever and rapidly progressive difficulty in breathing. In each of their cases the X-ray picture was compatible with pulmonary edema but was not supported by physical findings of congestive heart failure. Each patient had a rapid downhill course with fever, cyanosis, and air hunger. A complicating cardiovascular disorder in our patient was considered but dismissed as a cause of his symptoms because of a normal heart size, normal circulation time, and absence of any significant history of cardiac disease. We wonder if the circulation time might have been prolonged if done with the patient sitting up. In this position occlusion of the mitral orifice by the tumor mass may have been significant. Supine, the arm to tongue circulation time was clearly normal.

Mitral stenosis was the most commonly associated cardiac valvular lesion in patients with fatal influenzal pneumonia during the pandemic of 1957-1958.[1] It was felt that the pulmonary hypertension associated with mitral stenosis played an important role in the pathogenesis of fatal interstitial pneumonia.[3] The presence of intimal plaques in the pulmonary vessels and secondary hemosiderosis in the lungs was evidence of pulmonary hypertension in our patient.

The clinical findings in a patient with left atrial myxoma can mimic mitral stenosis and the hemodynamic changes are not dissimilar. This striking similarity has prompted such eponyms as "mitral stenosis in facsimile" in the description of atrial myxoma.[4] It was interesting that this similarity could also be reflected in the malignant course of an associated viral pneumonia.

SUMMARY

A case of left atrial myxoma complicated by a fatal abacterial pneumonia is presented. It is reminiscent of the malignant course of cases of mitral stenosis in the 1957-58 influenza pandemic.

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A History of Radiology in North Dakota

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When GIBBON described the reign of Antoninus as "marked by the rare advantage of furnishing few materials for history," he might have been describing the early history of radiology in North Dakota, so sparse is the written record.

Since 1955, diligent search for the date of the installation of the first X-ray machine in North Dakota has proved fruitless. A brief survey of the various city newspapers of the period disclosed only that the installation of these machines was not considered newsworthy enough to justify the extensive research involved. Through the courtesy of THE JOURNAL-LANCET and Allen Stone of its staff, copies were obtained of all X-ray materials which appeared in *Northwest Medicine* for the years 1901 to 1915, but none of these references mentioned any X-ray installation in North Dakota during this period.

The physicians who first used X-ray have long since passed away. The firm which furnished the bulk of equipment in the early days was Noyes Bros. and Cutler of St. Paul. Their business records of the period have long since been discarded.

Mr. Fred Schaffer, one of their early salesmen has passed on. Mr. Leo Hennie, another one of their early representatives who started work in the X-ray field in 1911, is still living and is now 80 years old. A letter from Mr. Hennie relating some of his early experiences is included in this paper.

Mr. F. L. Pengelly came to Minneapolis in November 1914 as a representative of the Victor X-Ray Company for the area. Most of the information as to the early X-ray installations in North Dakota was obtained from Mr. Pengelly.

Since Mr. Hennie and Mr. Pengelly did not start in X-ray in North Dakota until 1911 and 1915, respectively, and the search for detailed information before this time proved fruitless, the history before 1911 is fragmentary.

This paper will be divided into 3 periods—from earliest information through 1914, from 1915 through 1933, and from 1934, the date of first certification of radiologists, up to the present time.

Grand Forks. The earliest dated evidence we have is of a static machine bought by Dr. G. E. Engstad of Grand Forks in 1889. This machine was purchased for treatment of various medical conditions, a form of treatment popular at the time. Soon after the announcement of Roentgen's discovery, Dr. Engstad obtained a gas X-ray tube and used the machine for production of X-rays. In 1924 this machine was given to the North Dakota Historical Society which exhibits it in Bismarck.

Minot. Dr. E. A. Crokat (licensed in July 1894) installed an X-ray machine in Minot in 1901. He left the state in 1906 and moved to California to specialize in dermatology.

Bismarck. Dr. Smythe owned a Wimhurst static machine earlier than 1907. His widow gave the author a gas tube in its original carton dated 1907, with the price, $10.50, also on the carton.

In 1899, Dr. E. P. Quain had seen an X-ray machine in operation when, as an intern in Anker Hospital, he had seen a Dr. Wheaton obtain the exact location of a bullet in the calf of a leg by use of X-ray. The subsequent removal was a simple procedure, and Dr. Quain was thoroughly impressed by the values of roentgenography. In 1904 or 1905, he went to Johns Hopkins Hospital for some training in the use of this technique and bought an X-ray machine and hand fluoroscope for his and Dr. Ramstad's use in Bismarck. The current for this unit was supplied by dry-cell batteries which weighed more than a hundred pounds. The unit would be moved from the office to the hospital when needed and was used almost entirely for fractures of the thinner parts of the body. No attempt was made to protect the operators. While J. K. Blunt was in high school between 1910 and 1913, he and a friend purchased an X-ray tube from the Electro Importing Company of New York. Probaby made in Germany, the tube was 6 in. in diameter. They used a 1 kw. transformer and induction coil with

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an electrolytic interrupter and also built a large Tesla coil. The primary coil was 2 ft. in diameter and wound with large-guage copper wire; the secondary coil was 5 ft. long and 12 in. in diameter and wound with 20-gauge wire. The only Tesla coil on the market at the time was one with a secondary coil of about 16 in. The boys ordered pitch from the same company and spent all winter reducing it until they had a glass capsule of active radium bromide, which they kept sealed in a lead box. A year after graduation, the other boy died and the equipment and radium bromide were sent to the University of North Dakota.

In the meantime, Dr. V. J. LaRose had taken over all the X-ray work for the Quain and Ramstad Clinic. When the young Mr. Blunt came in for treatment of an infected area on his chin, Dr. LaRose questioned him about his future plans. The boy had none, so he became the "sorcerer's apprentice" in 1914. His remembrances of the period are probably a good description of the X-ray world of the era. He remembers the earliest equipment to be a Snook machine with a motor generator, since the city had only direct current; later, a Kelly-Koett and a Victor apparatus were added. The operator wore a lead-impregnated apron, but no one else in the room, including the assistants, was protected. Mr. Blunt was the technician until 1916, when he left to go to dental school.

Fargo. Dr. Nils Tronnes was using X-rays in 1905. During his training in Oslo, Norway, he had seen Prof. Schiotz make a roentgenogram of the hand of the King of Norway. Afterward, using his own simple static machine, Dr. Tronnes made an excellent roentgenogram of a hand by an exposure of forty-five seconds on a Lummier plate.

In 1908 Dr. Tronnes was practicing with Dr. Sands, and they acquired a Scheidl-Western X-ray machine which was used regularly for radiography of the bones of the extremities. In 1910 Dr. Tronnes went to Cook County Hospital in Chicago to see a demonstration of the interrupterless machine made by Kelly-Koett Company of Covington, Ky. The representatives of the company were surprised that anyone from North Dakota would be interested; there were only 2 such machines in Chicago when Dr. Tronnes ordered the third one for this area.

The physics department of the North Dakota Agricultural College purchased an X-ray unit from Noyes Bros. and Cutler about 1906. A Prof. Keene was head of the department at the time. Dr. E. N. Darrow used this equipment in fracture cases.

The foregoing dates are relative and could not be fixed with absolute accuracy.

Because many of the cities in the state had electricity only at night, most of the installations had to be operated on batteries during the day. These were sometimes dry-cell batteries. Glass jar storage batteries were also used which were recharged during the night when city current was available.

Static machines had low output and could be used only for examination of the thinner extremities. Drs. LaRose and Smythe once cranked Smythe's static machine for thirty minutes in an attempt to make a plate of a fractured femur. The resulting exposure was insufficient to outline the femur.

Some of the early problems in X-ray work are well described in a letter from Mr. Leo Hennie dated June 19, 1964.

When I first installed X-ray equipment in North Dakota it was in the year of 1911. I installed most of the Snook X-ray machines that Mr. Fred Schaeffer sold in North Dakota. Mr. Schaeffer and I worked for Noyes Bros. and Cutler at that time. They were located on 6th and Sibley in St. Paul. I was with them for four years until I came to work for the Pengelly X-Ray Co. in Minneapolis in the latter part of 1915 or early 1916.

Back in the early days of 1904 I worked for Hollis Electric Co. in Minneapolis who handled the Scheidel-Western X-Ray coils of Chicago and accessories, also 6- and 7-in. X-ray gas tubes. I installed a Scheidel-Western X-Ray unit at St. Barnabas Hospital in Minneapolis that was equipped with 2 interrupters, one was a mercury turbine interrupter that made 3,600 interruptions per minute for "fluoroscopy work," and the other was a electrolytic acid interrupter that made about 8,000 interruptions per minute for "radiographic work." These interruptions energized the primary side of the induction coil to give us the high voltage of the secondary coils, then to the X-ray tube; the incoming line voltage for this unit was 110 v. direct-current line. A year or two later a 4-jar rectifier was added to the Scheidel-Western line so you could operate the above equipment on a 110 or 220 v. A.C. current.

A 5×7 or 8×10 hand fluoroscope was the only thing we had in those days for fluoroscopic work. The first ones made did not have any lead glass protection in it. Later on, Scheidel-Western made an upright wooden structure about the size of an ordinary door with a piece of aluminum fastened that covered a center opening of frame and with counter-weighted movable frame behind to hold the X-ray tube and lead shutters that could be controlled from the front of the fluoroscope. Also, in front there was a counter-weighted fluoroscopic screen of a greenish color which was also protected with a piece of lead glass. (Most of all the lead glass came from Belgium and sold for about 14c per square inch.) This screen frame hung down by 2 ropes in front of the patient. These fluoroscopic screens had to be covered by a black bag or cloth when not in use, as the light in the room or sunshine would shorten the life of the screen which would turn yellow, then brown, then lose all of its fluoresence.

We had no X-ray films in the early days, only glass plates. These plates came packaged in strong paper boxes, six 14 × 17 plates to a package that you would open in the darkroom. You would put one plate at a time into a black envelope and, secondly, into an orange-colored envelope to prevent light leaks when brought out into light X-ray room. This was placed under the patient, who was lying on a flat horizontal wooden table, and then the X-ray exposure was made. Sometimes the doctor or nurse or technician would turn the patient a little for a better position, and you could hear the glass break, so another glass plate had to be placed under the patient. There was more or less breakage of these glass plates and a lot of expense too. Special frames were built in hospitals to store all the exposed plates. Each one was filed in white envelopes with the case history and name. There would be hundreds and hundreds of pounds of glass stored away.

Most of the X-ray tubes in the early days were manufactured by McAllister Wiggin X-Ray Tube Co. of Boston, and also by Green & Baurer X-Ray Tube Co. of New York and Boston. Good 6- or 7-in. X-ray tubes at that time sold for $38 apiece. As these tubes changed in vacuum from exposures from the heat of the target, they would lose their penetration. Many hospitals would have 8 or 10 X-ray tubes hung in wooden brackets on the walls of the X-ray room and marked with adhesive tape on each tube as to its penetration—2, 3, 4, 5, and 6 in.

If a doctor or technician wanted to take a picture of a finger or hand, he would select an X-ray tube from the wall that had a 2-in. penetration, and if a hip picture was to be taken, they would select a tube from the wall hanger that had a 6-in. penetration, so there was a lot of X-ray tube changing and a loss of time in these early days. Sometimes a tube of 6-in. penetration or more would get so high in vacuum that you could not pass any milliamperes through it. We would take this tube down to the kitchen of the hospital and put it in the oven and let it bake for a couple of hours. That brought the vacuum down so we could use the tube for more exposures. In all these gas tubes, when an exposure was made, the lower half of the tube would light up a bright green color and in line with the slant of the target. The upper half of the tube was transparent.

Next came a new improvement in gas tubes. This tube had 2 small glass bulbs or chambers, with different chemicals in each, welded to the top of this 7-in. diameter X-ray tube. This tube was called a Snook-Hydrogen X-Ray Tube. One chamber of the tube was to "lower" the penetration and the other was to "raise" the vacuum. All the technician had to do was to put the negative side of the X-ray machine wire to either chamber of tube and give it a few milliamperes for a very short exposure, then remove the negative wire from chamber and put back the same wire to the regular negative end of X-ray tube.

With this tube, the hospitals could do away with all the X-ray tubes hanging on the wall.

Then came the big improvement in X-ray tubes, which is still used today in our modern equipment. That was the "hot cathode X-ray tube"—the Coolidge X-Ray Tube manufactured by General Electric Co. With this tube you could regulate the amount of milliamperage by filament regulator at the control stand.

About in the year 1912 or a little later came a very important improvement to the X-ray field. That was an autotransformer that was put inside at the bottom of the control stand, as it was very heavy with about a 30-button control handle on top of the control stand. With this unit you could regulate any voltage you wanted and hold it there, regardless of what milliamperes you used.

Before we had only a straight resistance control on our control stands, and it always changed your milliamperes when you moved the resistance control lever or handle one button either way. So we always had to pull the spark-gap cord to see what penetration we had. That was a lot of wasted time—doing all this testing before making an exposure.

First came the overhead high tension wires that were stretched tight from one wall to another about a foot from the ceiling with wooden broomsticks about 14 in. long at each end as good insulators for high voltages. A No. 12 rubber-covered wire was used, and the insulation would be cut off where the cord-reels hooks were too hang so that the cord-reels could be hooked up to the X-ray tube over the table. There were also high tension switches that were fastened to ceiling so you could select fluoroscopic or radiographic setting or select another room. In some places these wires had to go through partitions, and special paper insulators were used.

When fluoroscoping, and using about 80 kv., the cord-reels wires behind the fluoroscope would fluoresce, like a cats tail, and throw off nitrous oxide gas or ozone into the room.

Second, to overcome this ozone effect, the X-ray companies made up new corona-proof, high-tension switches and all nickel plated brass tube to replace all the high-tension wires that we used first. There was no more corona effect from this tubing. These brass tubings were ⅜ to ½ in. in diameter for radiographic and fluoroscopic work. For deep therapy X-ray, we used from ⅝- to 1-in. diameter tubing.

The third change, and best of all, was high-tension transmission from X-ray generator to X-ray tube by shock-proof cable which eliminated shocks to patients, doctors, and technicians and also did away with all interference with radio and television sets in hospitals and doctors' offices.

Germany had the first shock-proof cables on their own equipment way back in the year 1912. I saw one of their pamphlets on X-ray at Noyes Bros. and Cutler, St. Paul, at that time. In the early 1900s, static machines were all we had for light X-ray work. The first machines were cranked by hand at the speed of the rotating glass plates from 100 to 250 rpm. The rotating plates were made of single-strength glass and had about a 30 in. diameter shaft. To take pictures of extremities you would have to crank the machine for about ten minutes or so, hoping the patient did not move to spoil the glass plate negative. The later machines were operated by an electric motor with a rheostat to regulate the speed of glass plates.

The voltage of these machines was very high. That caused a lot of secondary rays to fog the X-ray plate. The milliamperage was very low—1 to 3 ma.

I think it was the year of 1918 that the new X-ray film came on the market, made by Eastman Kodak Co., Rochester, N.Y. The heavy glass plates made by Seed X-Ray Plate Co. and the Crammer X-Ray Plate Co. of the U.S. went out of business.

Gas tubes were very difficult to work with and erratic in performance. Mr. Pengelly states he would use at least 6 gas tubes installing the average unit and training the doctor how to use the machine. The doctor, of course, was in most cases his own technician.

According to Mr. Pengelly, some type of X-ray

equipment was in use in North Dakota up to 1915 in the following situations, not listed chronologically: Bismarck—Quain and Ramstad Clinic, St. Alexius Hospital, and Bismarck Hospital; Devils Lake—General Hospital, Mercy Hospital, and Dr. William Sihler; Dickinson—Dr. J. W. Bowen; Fargo—St. John's Hospital, Drs. Sand and Tronnes at St. Luke's Hospital, Dr. Paul Burton, Dr. Murdock McGregor, and Dr. Humphrey (induction coil); Grand Forks—Deaconess Hospital, St. Michael's Hospital, and Dr. G. E. Engstad (static machine); Jamestown—Dr. William A. Gerrish; Garrison—Drs. Stucke and Stucke; and Wahpeton—Drs. Batemen and Thompson.

Beginning with 1915 there was a sudden upsurge in interest in radiology in the state and between 1915 and 1920, some 35 installations of equipment were recorded. Some of these were replacements of antiquated machines; many were in new situations.

The man to whose recollections of the period we are most indebted is Mr. F. L. Pengelly, whose reminiscences of the period show the pioneer conditions under which radiology developed in the state. His own story of the period follows.

I came to Minneapolis from Philadelphia in November 1914 to represent the Victor X-Ray Company in the northwest states.

I shipped a complete X-ray machine to the North Dakota State Medical Convention held in the Elks Club in Bismarck in May 1915. At this convention, I met for the first time Mr. Fred Schaeffer, representing the firm of Noyes Bros. and Cutler of St. Paul. During the meeting, Mr. Schaeffer endeavored to convince me that I would have a very tough time trying to sell X-ray equipment against the competition of an old and experienced company like Noyes Bros. and advised me to apply for a position as salesman with Noyes Bros. and Cutler.

At that time, Noyes Bros. represented almost every manufacturer of X-ray equipment in America and up to that time controlled about 95% of all the available business.

The only exceptions were that Mr. William Painter of Minneapolis had a nonexclusive contract with the Snook X-Ray Company of Philadelphia and I had an exclusive contract with the Victor X-Ray Company of Chicago.

In 1915, four of the X-ray manufacturers merged. They were the Scheidel Western X-Ray and Coil Company of Chicago, the McAllister Wiggin X-Ray Tube Company of Boston, the Snook X-Ray Company of Philadelphia and the Victor X-Ray Company of Chicago. The new company was named the Victor X-Ray Corporation.

In 1916, I was given an exclusive contract to represent the merged companies in the northwest states. My experience, selling and servicing X-ray installations in the northwest were like all others operating forty years ago, mostly long hours and hard work.

Traveling was by local railway trains, sometimes mixed passenger and freight, arriving and departing on an average of once each twenty-four hours—frequently at most inconvenient times, such as the early morning hours.

Every installation meant staying on the job until the customer could make fairly satisfactory X-ray exposures and could process the plates reasonably well. You can appreciate that the difficulties encountered with beginners were sometimes discouraging.

I have at times tried to work in places where there was no running water available, hot or cold, and where the temperature in the only location available for processing was little above freezing. Not only the solutions but the developing trays as well had to be warmed to a proper temperature before being taken into the cold darkroom, and this procedure was repeated for every plate developed. Service required after the installation had been completed was a problem and always costly because of the cost of transportation and time consumed in traveling.

I recall traveling 500 mi. only to find that the water used to mix the developing solution had become contaminated. About thirty years ago, we sent Mr. Leo Hennie from Minneapolis to Butte, Mont., to find that the rheostat on an old Snook X-ray control was left on a dead button. If the operator had moved it one button forward or backward, a journey of over 2,000 mi. would not have been necessary.

In order to help our customers with their problems, we began giving short courses of instruction in operative technique, which included the use and care of the equipment and minor trouble shooting as well as processing and exposure techniques.

In North Dakota, the first public course of instruction in X-ray exposure and processing technique was given at St. John's Hospital, Fargo, in 1918. Mr. E. C. Jerman of Topeka, Kans., conducted this course. We had heard, through a mutual friend, of Mr. Jerman's ability to teach the fundamentals of X-ray technique with near-perfect control of all the factors involved and arranged with him to conduct 3 courses under our supervision—the first at the Sioux Falls Clinic, the second in our offices in the LaSalle Building, Minneapolis, and the third at St. John's Hospital, Fargo. Nearly 70 physicians and laboratory assistants attended these 3 courses.

Mr. Jerman later was selected by the Victor X-Ray Corporation to inaugurate and direct their new educational department, which he did until his death.

About 1917, we received a contract from the state to equip the state hospitals at Jamestown, Dunseith, and Grafton with X-ray installations. Our Mr. Hennie made the installation at Jamestown. When everything was ready, a number of inmates were selected to have X-rays. Most of these patients were strapped securely to the table and left there until films were exposed and developed. Finally, a patient was brought in, and because he was a trusty and considered quite rational, the technician decided it would not be necessary to strap him on the table. An X-ray exposure was made and taken into the darkroom for processing. Just as soon as the patient found himself alone, he made plans to vacate; when the technician and Mr. Hennie returned, there was no patient in the room. A check revealed that he had jumped through a glass window. There was a little blood and plenty of broken glass as evidence. He was found the following morning slightly frostbitten.

The situations in which Mr. Pengelly made installations in the period from 1915 to 1920 are listed below in approximate chronological order.

J. W. Vidal, Fargo
Drs. Roan, Fisher, and Strauss, Bismarck
Dr. H. G. Woutat, Grand Forks

Kenmare Hospital (Drs. Ewing and Ewing), Kenmare
Drs. Darrow and Weible, Fargo
Drs. John and Elizabeth Rindlaub, Fargo
Drs. Sand and Tronnes, Fargo
Drs. Baldwin and Miller, Casselton
Quain and Ramstad Clinic, Bismarck
St. Alexius Hospital, Bismarck
Drs. McQueen and Stromberg, Langdon
Dr. John Towey, Langdon
Drayton Hospital (Dr. H. M. Waldron), Drayton
Drs. Stucke and Stucke, Garrison
Drs. Flath and Flath, Stanley
St. Joseph's Hospital, Minot
Drs. Carr and Carr, Minot
Grand Forks Clinic, Grand Forks
St. Michael's Hospital, Grand Forks
Deaconess Hospital, Grand Forks
Dr. L. Almklov, Cooperstown
North Dakota State Hospital, Jamestown
North Dakota State School, Grafton
North Dakota State Tuberculosis Hospital, Dunseith
Drs. T. O. Moeller and D. H. Mekeague, Maddock
Dr. George Holt, Jamestown
Drs. Bowen and Nachtwey, Dickinson
Drs. Glaspel and Glaspel, Grafton
Drs. Countryman and Seuter, Grafton
Drs. Campbell and Williamson, Grand Forks
Drs. Witherstein and Wilson, Grand Forks
Dr. H. M. Erenfeld, Minot
Dr. G. Roy Ringo, Minto
Dr. George Spielman, Mandan

Grand Forks. In 1915, the Grand Forks Clinic was organized by Drs. Healy, Law, and Woutat. It was about this time or a little earlier that Dr. Woutat acquired his first X-ray equipment. Dr. Woutat's interest in X-ray diagnosis and treatment began about 1913 or 1914, and with the formation of the partnership, he took over the X-ray facilities not only at the clinic but also at Deaconess and St. Michael's hospitals. Dr. Woutat was the first man in the area to spend the bulk of his time on X-ray procedures. He read many films free in order to stimulate use of the procedure.

The next major step was the purchase in 1920 of 100 mg. of radium from Radium Chemical Company of New York. This consisted of two 25-mg. capsules in 0.5 mm. of silver and 1 mm. of brass; 3 gold 12.5-mg. needles which were approximately 27 or 28 mm. in length; and a 10-mg. varnish plaque. The original purchase has been added to and modified from time to time as techniques have changed.

In the mid-20s, the Grand Forks Clinic acquired the equipment which made possible medium voltage X-ray treatment. Before this, Dr. Woutat had done some therapy with old gas tube equipment but this was chiefly for dermatologic conditions. Epitheliomas and hemangiomas were treated with radium surface application and the occasional use of interstitial needles. Medium-voltage equipment extended the list of conditions to be treated, and everything from warts to lymphoblastomas, breast carcinoma, and deep-seated malignancies was subjected to X-ray treatment.

Fargo. Having acquired a Snook machine in 1914, when it was operated by Dr. Ralph Weible and Dr. E. M. Darrow, the forerunners of the Dakota Clinic included Dr. Kent Darrow as one of the partners in 1916, and he made X-ray his primary concern. Interested in therapy, he treated a 16-year-old patient for myelogenous leukemia. According to the record, the patient responded fairly well and lived for several years. Treatment was directed to the spleen, but neither the factors nor time involved can be definitely established.

This group practice was enlarged by the addition of Dr. Frank Darrow in 1919. He took over the X-ray department, and by 1921, when Dr. Hugo Rostal joined the group, the work had increased so that Dr. Darrow was in charge of X-ray diagnosis and Dr. Rostal was in charge of X-ray therapy. An Acme unit had been acquired, and later Westinghouse equipment was used.

In August 1916, an X-ray department was established in St. John's Hospital and equipped with what was probably a Snook machine. The department consisted of one diagnostic room and a darkroom located in the basement. No designated doctor was in charge, and staff men read their own roentgenograms.

After 1919, Drs. Frank Darrow, Clay, and Bottolfson did most of the X-ray diagnoses.

In 1920 the new Fargo Clinic building was completed. It adjoined St. Luke's Hospital and was equipped with a new Victor Universal machine.

Until the clinic had built its own building, Drs. Tronnes and Sands had had their offices on the fourth floor of St. Luke's where both of them worked regularly with X-ray in addition to carrying on a general medical and surgical practice. In 1919, Dr. T. P. Rothnem joined them to head their X-ray department. When the group moved into their own building, all X-ray work for St. Luke's moved with them. From that day until 1961, work for both the clinic's outpatients and the patients in St. Luke's was done in the clinic X-ray department.

Minot. Dr. Russell Gates was the first radiologist in Minot. He joined the Northwest Clinic in 1928 but moved to California in 1934.

St. Joseph's Hospital acquired X-ray equipment in 1922.

Jamestown. Dr. H. M. Berg became a radiologist in Jamestown in 1926, practicing general medicine and radiology. However, after further

training in radiology, he moved to Bismarck in 1929 to become radiologist at the Quain and Ramstad Clinic and the Bismarck Hospital.

Bismarck. Dr. Victor J. LaRose did most of the X-ray work at the Quain and Ramstad Clinic until in the early 20s. He also carried on an active urologic practice.

Dr. A. J. Halgren assisted him in the X-ray work in the early 20s. After Dr. Halgren moved to Wisconsin, Dr. R. H. Waldschmidt joined the clinic in 1923. He did most of the X-ray work until in 1929. Dr. Waldschmidt also practiced urology and surgery during this period.

In 1929, Dr. H. Milton Berg joined the Quain and Ramstad Clinic as radiologist. This involved not only the radiological work at the clinic but also that for the Bismarck Hospital and for Quain and Ramstad patients who were at St. Alexius Hospital.

Various types of equipment had been acquired, and when Dr. Berg became radiologist he had as working tools the standard equipment of the period plus radium, which had been acquired by the clinic in 1918. Soon after his appointment, the clinic acquired a deep X-ray therapy unit and the clinic and hospitals modernized their radiology departments.

General considerations. It is obvious from Mr. Pengelly's list that many doctors all over the state were utilizing X-ray equipment in the late teens and the twenties. Naturally much of the work was done in the clinics and hospitals in the large centers of Bismarck, Fargo, Grand Forks, and Minot. The uses of X-ray expanded very rapidly and became so complicated that many doctors began specializing in the field, taking additional training in large teaching centers and abroad.

The expansion of radiology necessitated full recognition of this specialty; therefore, in 1933 the American Board of Radiology was established. Many of the doctors who were already specializing went on to become certified radiologists.

Grand Forks. At the death of H. G. Woutat in 1935, P. H. Woutat became the radiologist at the Grand Forks Clinic. The first 200-kv. treatment unit was installed late in 1936 and accurate calibration of the equipment was instituted. In 1949 arrangements were made for Dr. Woutat to supervise all phases of the radiographic work in St. Michael's Hospital, and in 1951 the same arrangement was set up in the Deaconess Hospital. Dr. Phil R. Berger was in charge of the actual work in both hospitals from 1949 through 1951. Opening of the therapy department was considerably delayed but was finally accomplished in June 1954.

Dr. R. Douglass Doss started the independent practice of radiology in Grand Forks in the late 50s.

Fargo. St. John's Hospital moved the X-ray department from the basement to the fifth floor of the hospital. The radiologist from the Dakota Clinic did the radiological work at St. John's until 1961. Since then the hospital has had its own radiologist, Dr. T. L. Donat. In 1955, a school for the training of X-ray technicians was established. In 1964, Dr. H. A. Ohrt joined the staff as Dr. Donat's associate.

Dr. Leo Nash who was trained in radiology at the University of Minnesota joined the Dakota Clinic in 1940 and remained until 1946 when he moved to St. Paul.

Dr. Fred Hewes, trained in radiology and a diplomate of the American Board of Radiology, joined the Dakota Clinic in 1946 and headed the radiology department until 1947. Since 1947, Dr. T. L. Donat has been in charge of the department. In 1953, Dr. Marshall Landa joined the department. In 1961, Dr. T. L. Donat disassociated himself from the Dakota Clinic but continued to be the radiologist at St. John's Hospital.

As the Fargo Clinic grew and the demand for X-ray services increased, Dr. Rothnem modernized the department, renovating with new shockproof equipment and adding the new 200-kv. Westinghouse deep therapy machine. This was in 1934 and 1935. In 1941, Dr. Rothnem became seriously ill and Dr. L. A. Nash, who was radiologist at St. John's Hospital, carried Dr. Rothnem's work for about six months.

In April 1942, Dr. Charles Heilman, having completed his fellowship in radiology at the Mayo Clinic, came to head the department at St. Luke's and the Fargo Clinic. In 1950, Dr. Richard Storrs joined the department, but after a year and a half he returned to Syracuse. He was succeeded by A. G. Skjelset, who was trained under Dr. H. Milton Berg at Bismarck and under Dr. Leo Rigler at the University of Minnesota.

Since Dr. Skjelset had not served any time in the service, he decided to complete this obligation and left the Fargo Clinic. He was replaced by Dr. Lester Shook. Dr. William M. Blackwell and Dr. Richard Gross joined the staff in the early 60s. After a short time Dr. Gross left and moved to Ohio. Dr. Blackwell has also left the staff recently.

In April 1953, the department moved to new quarters on the ground floor of the Fargo Clinic with all new diagnostic and therapy equipment. Beside the standard procedures, the specialized

services required by neurosurgeons, cardiologists, chest surgeons, and so on, are provided. A complete, separate radiological department was installed in the St. Luke's Hospital in 1961.

Minot. The Northwest Clinic was without a radiologist from 1934, when Dr. Russell Gates left, until 1937 when Dr. Willard Wall took over. Dr. Marianne Wallis was the first radiologist at St. Joseph's Hospital, although they had been doing radiological work since 1922. Dr. Wallis came in December 1951.

Jamestown. The first board-certified radiologist in Jamestown was Dr. John M. Hewitt who joined the DePuy-Sorkness Clinic about 1948. He also did most of the work at the 2 hospitals. After Dr. Hewitt moved to South Dakota he was succeeded by Dr. Paul F. Christiansen who later moved to Montana. He was succeeded by Dr. Sam Miller, who died of a heart attack Oct. 13, 1955. Later, Dr. John J. Jestadt joined the DePuy-Sorkness group and also became the radiologist at the 2 hospitals; he moved to Boise, Idaho, in early 1964.

Dickinson. In 1955, Dr. Richard F. Raasch became the first board-certified radiologist in Dickinson. He does the radiological work for the various groups and individual doctors in Dickinson for the hospital there and also visits some of the community hospitals in the surrounding towns.

Bismarck. The Quain and Ramstad Clinic had been building in size and volume, and after 1933, it began developing many specialized techniques.

In 1944 a radiological residency program was set up in connection with the Bismarck Hospital and the University of Minnesota. The residents spent the first year and a half at the University of Minnesota and the last half of the training period in Bismarck, their time being divided between the Bismarck Hospital, St. Alexius Hospital, and the Quain and Ramstad Clinic. In the latter part of 1947, the University of Minnesota discontinued these combined residencies, but a full three-year radiological residency program was approved the same year in the name of the Bismarck Hospital. Since the residents spent an equal time at both Bismarck and St. Alexius hospitals, in 1959 the name of the program was changed to the Bismarck Associated Hospitals Residency.

The following doctors received their training in radiology under the combined program with University of Minnesota and Bismarck Hospital: Edward M. Anderson of LaCrosse, Wis.; George S. Boyer of Weslaco, Texas; Richard B. Bridenbaugh of Billings, Mont.; and Fredrick M. Reis of Mattoon, Ill.

The following men received all or part of their training in the Bismarck Associated Hospitals Radiology Residency Program: Roger M. Berg, Bismarck; Abuzer Berilgen,* Saskatoon; Arthur G. Dodds, Walla Walla, Wash.; John J. Jestadt, Jamestown, N. Dak.; Wesley Levi, Boise, Idaho; Robert Olson, Williston, N. Dak.; Pablo Ramos, Bismarck; Ali Sener, Turkey; Arlo G. Skjelset,† Great Falls, Mont.; Eric W. Walter, Wooster, Ohio; and John R. Williams, Rutland, Vt.

The following men are at present taking a radiology residency at the Bismarck Associated Hospitals: William F. McCullough, William J. Porter, and Donald J. Schmidt.

In 1942, one of the staff at the Quain and Ramstad Clinic developed multiple myeloma, and the clinic obtained it first isotopes. Isotope P^{32} was used for relief of pain. These isotopes were obtained through the famous Lawrence brothers, John and Ernest, who were North Dakota emigrants working in California. In 1953, the clinic obtained its Atomic Energy Commission license to use isotopes generally and currently use I^{131}, P^{32}, AU^{198}, and $CrP^{32}O_4$, colloidal chromic phosphate.

A 1,000 curie cobalt teletherapy unit was installed in the Bismarck Hospital in 1957. The hospital, with financial assistance from the John A. Hartford Foundation, Inc., installed a room completely equipped for cardiac and neuroradiological studies in 1960.

In 1949, Dr. John R. Williams joined the radiological staff at the Quain and Ramstad Clinic and the 2 Bismarck hospitals. In the mid-50s, Dr. Williams decided to return to Vermont. He was replaced by Dr. Johan Eriksen, who had his radiological training in Norway and who has become a valuable addition to the staff.

Dr. James F. Nelson was also on the staff for a few months in the late 50s. Drs. Wesley Levi and Robert J. Olson, after completing their residency at the Bismarck Associated Hospitals, remained on the staff for from one to two years.

Drs. Roger Berg and Pablo Ramos were added to the staff after completion of their training in Bismarck.

The radiological staff at the Bismarck Hospitals and at the Quain and Ramstad Clinic, at the present time, therefore, consists of Drs. H. Milton Berg, Johan Eriksen, Roger M. Berg, and Pablo Ramos.

General considerations. The year 1942 was important in the history of radiology in the state since it marked the organization of the North

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*Dr. Berilgen took one and one-half years and then transferred to the University of Saskatoon to complete his training.
†Deceased

Dakota Radiological Society. The first members were: Dr. H. M. Berg, Quain and Ramstad Clinic, Bismarck; Dr. Charles Heilman, Fargo Clinic; Dr. Leo Nash, Dakota Clinic, Fargo; Dr. W. W. Wall, Northwest Clinic, Minot; and Dr. Philip Woutat, Grand Forks Clinic.

By September 1963 the group had more than tripled to include the following: H. M. Berg, Bismarck; Roger M. Berg, Bismarck; William Blackwell, Fargo; Theodore L. Donat, Fargo; R. Douglas Doss, Grand Forks; Johan Eriksen, Bismarck; Charles O. Heilman, Fargo; John J. Jestadt, Jamestown; Marshall Landa, Fargo; Robert J. Olson, Williston; John H. H. Penners, Grand Forks; Richard F. Raasch, Dickinson; Pablo Ramos, Bismarck; Lester D. Shook, Fargo; Williard W. Wall, Minot; Marianne Wallis, Minot; and Phillip H. Woutat, Grand Forks.

In 1946, the North Dakota State Health Department decided to set up a miniature chest survey program in the state. The North Dakota Radiological Society agreed to interpret the films and to pool the proceeds from this activity in a treasury for the society to use for educational and scientific purposes. This provided funds for several projects.

A student loan fund of $6,000 was set up for the North Dakota Medical School at Grand Forks. For many years the society furnished an outstanding radiologist for the program of the annual meeting of the North Dakota State Medical Society. On several occasions the society also sponsored a dinner meeting during the annual medical society meeting to which were invited, as guests of the radiologists, all members of the state medical association who wished to attend. The guest radiologist would speak at this meeting, also.

Occasionally, funds have been provided for a winter meeting of the radiological society with an outstanding speaker. Among the speakers who have thus been brought to North Dakota are Drs. Chauncey N. Borman, John Caffey, George D. Davis, Juan A. del Regato, Sven Roland Kjellberg of Gothenburg, Sweden, Joseph Jorgens, H. Dabney Kerr, Per Odman of Stockholm, Sweden, Harold O. Peterson, William Peyton, Leo Rigler, Lawrence L. Robbins, Ulf Rudhe of Stockholm, Sweden, and Harry Weber.

At the request of the Continuation Center and the department of radiology of the University of Minnesota, the North Dakota Radiological Society entertained Dr. Merrill C. Sosman and Fred Jenner Hodges on a pheasant and duck hunting trip.

Other uses of the fund have been to acquire educational materials in the form of books and slides for members' use in study and lectures and to help finance the annual meeting of the North Dakota Society of X-ray Technicians.

The author wishes to thank the following for their generous contributions to this history: Theodore L. Donat, M.D., Charles Oliver Heilman, M.D., Leo Hennie, Marianne Wallis, M.D., Philip Henry Woutat, M.D., Mr. J. K. Blunt, and Mr. F. L. Pengelly.

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LESLIE J. SCHOENFIELD, M.D., and WILLIAM T. FOULK, M.D., Mayo Clinic and Foundation, Rochester, Minn. Studies of sulfobromophthalein sodium (BSP) metabolism in man. II. The effect of artificially induced fever, norethandrolone (Nilevar), and iopanic acid (Telepaque). J. clin. Invest. 43:1419-1423, 1964.

Transactions of the North Dakota State Medical Association

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WARREN R. JENSEN, M.D. ..... Valley City
A. M. CAMERON, M.D. ..... Minot
KENNETH HELENBOLT, M.D. ..... Grand Forks
R. J. ULMER, M.D. ..... Fargo

5. *To Consider Reports of The Committee on Medical Economics, including Advisory Committee to Public Assistance Division of State Welfare Board, Committee on Rural Health and Governor's Health Planning Committee:*

E. G. VINJE, M.D., Chairman ..... Hazen
HENRY A. NORUM, M.D., Vice-Chairman ..... Fargo
C. G. JOHNSON, M.D. ..... Rugby
JOHN A. SANDMEYER, M.D. ..... Grand Forks
RICHARD S. LARSON, M.D. ..... Velva
DONALD E. SKJEI, M.D. ..... Williston

6. *Committee on Resolutions to Include New Business:*

R. C. PAINTER, M.D., Chairman ..... Grand Forks
J. N. ELSWORTH, M.D., Vice-Chairman ..... Jamestown
L. A. GILTNER, M.D. ..... Minot
PHILLIP O. DAHL, M.D. ..... Bismarck
W. C. HANEWALD, M.D. ..... Dickinson
PAUL J. BEITHON, M.D. ..... Wahpeton

7. *Committee on Credentials:*

DONALD E. SKJEI, M.D., Chairman ..... Williston
(Also serves on Committee No. 5)
ROBERT H. DeLANO, M.D., Vice-Chairman .... Northwood
(Also serves on Committee No. 3)

PROCEEDINGS: HOUSE OF DELEGATES SEVENTY-EIGHTH ANNUAL MEETING OF THE NORTH DAKOTA STATE MEDICAL ASSOCIATION

Grand Forks, North Dakota — May 1, 1965

The First Session of the House of Delegates of the North Dakota State Medical Association was called to order by the Speaker of the House, Dr. Lee Christoferson, at 3:00 P.M. in the Dacotah Hotel, Grand Forks.

Dr. Skjei, Chairman of the Credentials Committee, reported that all credentials were in order and there were twenty-eight delegates and three alternate delegates, duly authorized, and present.

Secretary Buckingham called the roll and the following delegates and alternates responded:

Doctors: H. A. Norum, Fargo; M. H. Poindexter, Fargo; A. C. Burt, Fargo; R. E. Kulland, West Fargo; Paul Beithon, Wahpeton; Blaine Amidon, Fargo; R. J. Ulmer, Fargo; R. D. McBane, Alternate, Devils Lake; R. C. Painter, Grand Forks; J. A. Sandmeyer, Grand Forks; G. L. Countryman, Grafton; R. H. Leigh, Grand Forks; K. S. Helenbolt, Grand Forks; W. T. Powers, Alternate, Grand Forks; L. A. Giltner, Minot; R. S. Larson, Velva; A. M. Cameron, Minot; Jens Sahl, Minot; Warren Jensen, Valley City; P. O. Dahl, Bismarck; J. J. Moses, Bismarck; R. B. Tudor, Bismarck; M. A. K. Lommen, Bismarck; C. J. Baumgartner, Bismarck; E. G. Vinje, Bismarck; E. O. Hieb, Jamestown; J. V. Miles, Jr., Alternate, Jamestown; D. E. Skjei, Williston; R. E. Hankins, Mott; W. C. Hanewald, Dickinson; J. M. Little, Mayville.

The following also attended the House of Delegates meeting: Drs. G. A. Dodds, Amos Gilsdorf, J. D. Craven, G. W. Toomey, R. D. Nierling, Thomas Pederson, E. H. Boerth, W. A. Wright, C. J. Glaspel, R. E. Mahowald, Keith Foster, W. M. Buckingham, R. W. McLean, C. H. Peters, Frank DeCesare, G. Christianson, Dean Strinden, W. R. Fox, J. M. Van der Linde, F. D. Naegeli, Blair Henningsgaard, Mr. Lyle A. Limond and Mr. Sherwood Williams.

Speaker Christoferson announced that the Association had the misfortune to lose seven members who had passed away during the past year. He asked the secretary to read the names of the deceased members and requested those in attendance to stand for a moment of silence in their respect. The names of the deceased members, as read by Secretary Buckingham: Drs. J. Van Houten, Valley City; J. J. Korwin, Williston; H. J. Meunier, Oakes; W. F. Sihler, Devils Lake; D. D. Rubbert, LaMoure; G. R. Lipp, Bismarck; Agnes Stucke, Garrison.

The motion was made by Dr. Painter, seconded by Dr. Hankins, that the reading of the minutes of the December, 1964 meeting of the House be dispensed with, and that they be approved as written in the Handbook. Motion passed.

Dr. Christoferson asked that all reports, as printed in the Handbook, be referred to the proper reference committee for their study, and these reports, in turn, be introduced as part of the business during the afternoon session the following day. He advised the members that all resolutions made by the committees must be forwarded to Resolutions Committee No. 6. He added the resolutions would then be presented to the House by the members of that committee.

REPORT OF THE PRESIDENT

To have had the honor to serve as your president in the past year has been a rewarding privilege. Our society has made some advancements in the pattern of medical care and has maintained previous gains.

I wish to use this report as a medium to thank all of the District and State Society officers, the Council, the House of Delegates, the Committee Chairmen and their members for the time expended. The strength of our Society is due solely to the energies of these groups. The experienced help and guidance furnished by Mr. Lyle Limond, Executive Secretary, Mr. Daniel E. Buchanan, Director of Public Information, our capable central office staff—Margaret Fremming and Myrtle Kohler are gratefully appreciated. Our Association should be made aware of the long, tedious hours spent by Lyle Limond in our interest during the recent legislative session. I have nothing but commendation for his efforts. A note of thanks is due my immediate professional associates who have taken over my duties when I was absent during the functions of this office.

A detailed report of your president's travels and activities is not deemed relevant. It is sufficient to say that I have attended those meetings, and participated in the activities that would contribute the greatest reward to our Society at county, state, and national level. Your president-elect, Dr. Joseph Craven, has been most helpful to me in meeting some of the demands of this office. The greatest pleasure has been derived from the visits to the District Society meetings—I have appeared at these whenever invited to do so. All of the District Societies except one were visited during the past year.

At the San Francisco A.M.A. Meeting in June, 1964, an organization was formed consisting of all State Society Presidents, the Presidents-Elect, and the Immediate Past Presidents. The purpose of the group is the exchange of information between state medical societies in the solution of mutual problems, and the transmission of policy opinions to the A.M.A. The Board of Trustees of the A.M.A. arranged for a second meeting of this group at Chicago in August. This organization fills a void and will provide beneficial action in the future. I would urge all future presidents and presidents-elect to actively participate in this organization. It should provide excellent training and background for the president-elect.

Observations this past year have resulted in the formulation of the suggestions enumerated below, which your president feels will be of future benefit to our medical society.

1. The office of State Society President is no longer a one-year function. It is a two-year office beginning as president-elect. It is essential that this officer participate actively in our state medical business, and be given certain assignments; thus, in these changing times a more

valuable president will be produced. To further this recommendation, I suggest that $200 be allotted, by the Council, to the president-elect to help defray travel expenses.

2. Our state medical society should establish a voluntary effective areawide hospital planning agency. If this is not done, the state may well establish a law giving that government final say on all hospital construction. Unfortunately, this has already become a reality in the state of New York.

3. Our fifty year awards to faithful practitioners in our state is a most excellent recognition, but totally unrealistic. With present educational time demands and emerging patterns of practice this goal is recognized too late. I suggest that consideration be given to making this award at forty years after graduation from medical school.

4. Our medical society has an official representative on the Blue Shield Board of Directors. However, a report is never published in the delegates' handbook. I feel that in these crucial times it is of paramount importance to have a close liaison between Blue Shield and our House of Delegates. It is suggested that in the future the report from our representative be published in the delegates' handbook and that it be considered by an appropriate reference committee of the House.

In conclusion, I should like to salute the physicians of our state for their unselfish dedication and their able participation in medical society affairs. It is a privilege to be one of this group and I thank each of you for the rewarding year bestowed upon me.

Respectfully submitted,
(Signed) G. Alfred Dodds, M.D., *President*
North Dakota State Medical Association

REPORT OF THE SECRETARY

The following report of the Secretary is respectfully submitted:

MEMBERSHIP: The total membership for 1964 was 491. Of this number, 454 paid the regular membership fee, 1 paid one-half year's dues, 5 were on a limited basis, 3 were retired and 27 were Honorary members. One member was carried on a complimentary basis due to illness. Seven physicians passed away during the year and several have left the state. New members, however, are being steadily added to our roster.

Table 1 shows the annual membership for the past five years.

TABLE 1
COMPARISON OF ANNUAL MEMBERSHIP

	1960	1961	1962	1963	1964
Paid memberships	418	436	436	449	455
Honorary memberships	24	26	25	21	27
Limited and retired	5	3	4	6	8
Dues cancelled (age exemption, illness, military service)	4	1	1	1	1
	451	466	466	477	491

Table 2 shows the annual dues payments according to the cut-off date for preparation of this report for the past five years. The cut-off date of April 2, 1965 has given members a grace period of five weeks in which to pay their current dues, even though the Constitution and By-Laws of the Association state that all assessments must be forwarded to the Secretary not later than the 1st day of March of each year. You will note that even with the extension of time and despite the fact that members were urged to make dues payments as early as December, quite a large number of members are delinquent in dues payments.

TABLE 2

	April 17 1961	May 1 1962	April 12 1963	April 3 1964	April 2 1965
Paid-up members	348	374	388	412	412
Honorary members	27	25	21	25	22
To be honorary	2	2	1	1	3
Dues cancelled	2	1	–	1	–
Limited	1	–	2	3	3
Retired	–	–	2	2	5
	380	402	414	444	445

STATE ASSOCIATION MEMBERSHIPS

1964—Total Membership 491

District	Reg.	Rtd.	Ltd.	Comp.	Hon.
First	103	1	1	–	2
Second	37	–	–	–	3
Third	80	1	1	–	3
Fourth	61	–	–	–	5
Fifth	8	–	–	–	2
Sixth	82	1	1	1	6
Seventh	32	–	1	–	2
Eighth	19	–	–	–	–
Ninth	25	–	–	–	4
Tenth	8	–	1	–	–
	455	3	5	1	27

1965—Total Membership 442

District	Reg.	Rtd.	Ltd.	Comp.	Hon.
First	83	1	–	–	2
Second	38	–	–	–	2
Third	66	1	2	–	3
Fourth	57	–	–	–	4
Fifth	9	–	–	–	1
Sixth	80	1	1	–	5
Seventh	28	2	–	–	1
Eighth	21	–	–	–	–
Ninth	23	–	–	–	4
Tenth	7	–	–	–	–
	412	5	3	–	22

A.M.A. GENERAL MEMBERSHIPS

	1964	April 2, 1965
First District	104	86
Second District	38	38
Third District	84	70
Fourth District	63	55
Fifth District	10	10
Sixth District	87	85
Seventh District	35	32
Eighth District	18	19
Ninth District	27	24
Tenth District	9	7
	475	426

Representation in the House of Delegates is based on one delegate for each 15 paid-up members (or major fraction thereof), together with Honorary members. Delegates from the local societies should be seated on this basis so it is essential that dues be forwarded promptly.

The continued cooperation on the part of all members will be greatly appreciated.

Respectfully submitted,
(Signed) Wm. M. Buckingham, M.D., *Secretary*
North Dakota State Medical Association

HOUSE OF DELEGATES SPECIAL SESSION

A special session of the House of Delegates was called to order by the Speaker, Dr. Lee Christoferson, on Sunday, December 13, 1964, at 10:15 A.M., Gardner Hotel, Fargo, North Dakota.

Dr. William Buckingham, Secretary, called the roll and the following Delegates responded:

DOCTORS: A. C. Burt, H. A. Norum, R. J. Ulmer, M. H. Poindexter, Jr., R. E. Kulland, Paul Beithon, B. F. Amidon, A. Malcolm Cameron, R. S. Larson, P. O. Dahl, M. A. K. Lommen, R. E. Hankins, G. H. Hilts, R. C. Painter, John Sandmeyer, George Countryman, Richard H. Leigh, Kenneth Helenbolt, Lloyd Giltner, Jens Sahl, Jr., C. J. Klein, R. B. Tudor, John Elsworth, James Little.

Alternates present were:

DOCTORS: W. T. Powers, Donald C. Oliver, and Ralph Dunnigan.

The speaker appointed the following persons to serve as delegates in the absence of a regular delegate or alternate from their respective societies: Drs.: W. R. Fox, and James Moses.

The Secretary indicated that a quorum existed.

OTHERS PRESENT: G. A. Dodds, M.D., T. E. Pederson, M.D., R. E. Mahowald, M.D., A. R. Gilsdorf, M.D., R. W. McLean, M.D., F. A. DeCesare, M.D., V. J. Fischer, M.D., T. H. Harwood, M.D., C. H. Peters, M.D., Hubert Carbone, M.D., A. C. Kohlmeyer, M.D., Wm. Daner, Lyle Limond, Daniel Buchanan, Margaret Fremming, Myrtle Kohler.

Dr. Dahl made a motion that the reading of the minutes of the last meeting of the House of Delegates be dispensed with. Seconded and carried.

Dr. Christoferson advised the members that a motion would be needed before there could be any discussion from the floor.

The Speaker went on to suggest that, since the House was dealing primarily with matters of Association legislative policy, they might want to table an occasional bill for action in the afternoon, thereby allowing further time for thought and discussion during the noon hour.

Dr. Dodds was introduced, and advised the members of the House that, as the governing body of the Association, all due deliberation on any action should be taken. He added that he felt a strong and positive approach should be taken toward legislative matters, with special emphasis on the Kerr-Mills Law.

At this time, Dr. Pederson spoke briefly to the House concerning an address given at a recent AMA meeting in Miami by Donovan Ward, M.D., President of the American Medical Association. He felt that this address had been most exciting and dramatic and he urged every member of the House to read this talk upon its publication in the AMA News and the Journal of the AMA.

Dr. Pederson apprised the House that it would be his pleasure to place the name of Willard A. Wright, M.D., Williston, in nomination for President-Elect at the June 1965 meeting of the American Medical Association in New York City. He added that many members of the House of Delegates of the AMA had urged Dr. Wright to place his name in nomination. Dr. Pederson further stated that he felt this was a distinct honor for North Dakota, and asked the House of Delegates to give unanimous support to Dr. Wright's candidacy as President-Elect of the American Medical Association.

Dr. Christoferson reminded the Delegates of a proposed change in Chapter 2—Section 1 of the By-Laws, tabled by the House in May, 1964. He noted that, according to Chapter 14 of the By-Laws, it is mandatory for the House to table proposed amendments for action at any later session. A motion was passed to untable the proposed change in the By-Laws which deals with the length of annual meetings. Another motion was passed to amend Section 1 of Chapter 2 of the By-Laws to read:

> Section 1. The annual session shall be held for *three* consecutive days beginning on a *Friday*, which period of time should include the first Sunday in May. (This change was adopted unanimously by the House).

It was pointed out, however, that the change be implemented in 1966, or as soon as practicable.

The next item of business concerned proposed changes to the present law on District Health Units. The motion was made by Dr. Tudor, seconded by Dr. Giltner, that the House not approve the bill as presented.

Among the points made during the discussion of this motion, was the Council's opinion, as expressed by Dr. Mahowald, that the language which requires a physician to serve on a District Board of Health be retained. Dr. Tudor's motion was defeated.

It was then moved by Dr. Painter and seconded by Dr. Powers, that the House approve the proposed changes in the District Health Unit Law in principle, with the recommendation that a physician be included on District Boards of Health. Dr. Painter's motion was subsequently amended to read that the House approve in principle the proposed additions to the District Health Unit Law, with its objection to the deletion of the language which requires that a physician serve on a District Health Unit Board. The amended motion prevailed.

Proposed legislation on the Battered Child was next brought to the attention of the House.

A motion to approve the Battered Child Bill in principle, as drawn by the Legislative Research Committee was made by Dr. Powers. This motion was seconded by Dr. Tudor and carried.

House consideration was next directed to the request by the State Hospital for funds from the State with which to construct an Adolescent Treatment Center on the hospital grounds.

Dr. Tudor made a motion that the House approve in principle a 100-bed Adolescent Treatment Center proposed for the State Hospital. This motion was seconded by Dr. Hilts, and carried.

During discussion of the motion at hand, Dr. Carbone, Superintendent of the State Hospital, and Dr. Kohlmeyer, Chairman of the Mental Health Committee, described the advantages of such a center and urged favorable action by the House on the proposal.

The next item introduced to the House for consideration was the 1963 Institutions Transfer Bill (SB 320) transferring the administration of the State Hospital and the Grafton State School to the Mental Health Division of the State Health Department, and the San Haven Sanatorium to the State Health Department.

Dr. Buckingham reported to the House that the transfer of these Institutions from the Board of Administration was supported in principle by the Legislative Committee, the Council and the Mental Health Committee.

It was moved by Dr. Beithon, seconded by Dr. Lommen, that the House of Delegates approve, in principle, the transfer of Institutions from the Board of Administration as set forth in Senate Bill 320.

Both Drs. Kohlmeyer and Christoferson noted that it is likely several bills to transfer State Institutions from the Board of Administration would appear in the 1965 legislature. Consequently, it was Dr. Christoferson's feeling that the House give the Committee on Legislation adequate guidance in dealing with various transfer bills.

Mr. Daner, Association legal counsel, explained that the Board of Administration presently has jurisdiction over all the State's charitable and penal institutions. He, too, spoke of a growing interest among many in transferring these institutions from control by the Board of Administration.

Dr. Dahl, in speaking of SB 320, reminded the dele-

gates of the difference between transferring an institution to the Mental Health Division of the State Health Department, and transferring it to the State Health Council, the body responsible for the entire operation of the Health Department.

Dr. Peters said the Council felt any such transfer should be to the State Health Council. The Council further suggested there be a Medical Advisory Committee to the State Health Council to help set medical policy on patient care in the State Institutions, should they be transferred.

A motion to table discussion of the Institutions Transfer Bill was offered by Dr. Countryman, seconded by Dr. Leigh, and carried.

The next item of business brought before the House was the subject of community mental health service units. Dr. Buckingham explained that both the Committee on Legislation and the Council approved of such units in principle.

The motion was offered by Dr. Beithon, seconded by Dr. Cameron, that the House approve of the establishment of community mental health service units, as embodied in an amended version of the 1963 Legislature's House Bill 813.

Dr. Christoferson granted the floor to Dr. Carbone of the State Hospital who stated that he felt there was a need for community mental health service units. Advantages cited by Dr. Carbone included: the availability of care closer to the client's home; a follow-up service for persons discharged from the State Hospital; and the obvious advantage of earlier diagnosis and treatment for persons in need of care.

Dr. Kohlmeyer concurred with Dr. Carbone, adding that the Committee on Mental Health had considered this subject in detail the previous Friday night, and strongly recommended House approval of such units.

There was a good deal of additional discussion about Dr. Beithon's motion and questions raised about such matters as referral policies, the selection of staff, the amount of time a psychiatrist would spend there, etc. Dr. Peters suggested that perhaps a Medical Advisory Committee would be desirable to assist the Mental Health Division of the State Health Department in setting standards for the proposed Community Mental Health Service Units.

A motion was offered by Dr. Hankins to table further discussion of the subject under consideration. It was seconded by Dr. Dunnigan. However, this motion failed to carry.

It was finally decided that the establishment of Community Mental Health Service Units seemed a certainty, and medicine might best serve to attempt to incorporate its best thinking into such legislation. It was also pointed out that such units could provide a referral facility not now available to many physicians in the State.

On a call for the question, Dr. Beithon's motion was passed.

The matter of an amendment to the Cancer Quackery Law was next introduced to the members of the House.

Dr. Buckingham pointed out that both the Committee on Legislation and the Council had approved this amendment with the addition of "or dentist" after the word physician in the present Cancer Quackery Law. Dr. Dahl moved that the House concur with the proposed additions to the present law. This motion was seconded by Dr. Elsworth and carried.

Recess: 1:05 P.M.

The Speaker reconvened the House at 2:15 P.M. The first matter of business brought before the members was the section of the Privileged Communication Law concerning the Physician-Patient Relationship.

Dr. Buckingham made known to the House that both the Council and the Committee on Legislation had approved an amendment to this section of the Privileged Communication Law.

A motion was made by Dr. Kulland, seconded by Dr. Elsworth, that the House approve the suggested amendment to the Privileged Communication Law.

Mr. Daner, legal counsel to the Association, informed the members of the House that the law, in its present form, does not assure complete privileged communication between patient and physician. He fully recommended that the House accept the proposed amendment. Motion passed.

Following action on the Privileged Communication Law, the House next turned its attention to the Medical Center Loan Law. Dr. Buckingham informed the House that the Committee on Legislation had approved an amendment, but that the Council had taken no action. He explained that this amendment to the Medical Center Loan Law would liberalize and broaden the "forgiveness clause" in the present law to include interns, residents and faculty members at the UND School of Medicine.

Dr. Dahl moved that the House disapprove of the suggested amendment to the Medical Center Loan Law. Seconded.

In discussing Dr. Dahl's motion, Dr. Ulmer spoke for the Committee on Medical Education by saying they thought the "forgiveness clause" should be extended, since the present loan law was not proving significant in obtaining physicians for small communities. He went on to say that this amendment, drawn in 1963, was not introduced in the Legislature, for fear of placing the experience of the medical center loans under scrutiny which, he said, the fund could not stand. Dr. Ulmer asked the House to approve the recommendations of his Committee.

Asked his opinion of amending the loan law, Dr. Harwood felt strongly that "forgiveness" be extended at least to internships. He said it would not jeopardize the loan fund. Dr. Harwood also spoke briefly about the medical center mill levy itself, citing it as a significant factor in the present development of the School of Medicine at the University.

There was general agreement that measures to attract interns to the state whom communities could seek as physicians was of greater importance than attracting residents. There was some discussion that steps be taken to increase the number of internships offered in the state.

At this point, the motion proposed by Dr. Dahl was passed.

It was then moved by Dr. Leigh, seconded by Dr. Kulland that the Loan Fund Law be amended to provide "forgiveness" of loans to physicians or dentists who agree to practice in towns with 5000 persons or fewer, and to include "forgiveness" for physicians taking internships in the State. Carried.

The next item on the agenda was the consideration of proposed changes in the present Kerr-Mills (MAA) Law. Dr. Buckingham stated that both the Council and the Committee on Legislation had approved modification of this law.

Dr. Powers said that it was the feeling of the Legislative Committee that the Association go on record in attempting to extend our MAA program. The Legislative Committee proposed that the income limits be raised to $1500 single, and $2100 for a couple. The Committee also suggested that the allowable cash assets be raised

to $750 for a single person and $1500 for a couple. Dr. Powers also said that steps would most likely be taken to attempt to simplify the application procedures for assistance under MAA. He then moved the adoption by the House of the suggested changes to MAA. Dr. Larson seconded his motion. Carried.

The next order of business brought to the attention of the House was a request for endorsement of a free survey of X-ray facilities in physicians' offices by the Radiological Health Division of the State Health Department. The members were told that the Council had voted favorably toward this program.

A motion was made by Dr. Moses, seconded by Dr. Tudor, that the House of Delegates concur with the Council in its endorsement of the Health Department's program of voluntary X-ray survey. Carried.

The discussion of the 1963 Senate Bill 320 was untabled. Dr. Countryman told the House that he had contacted Dr. Rand of Grafton, and the latter was not inclined to be in favor of the bill. It was explained by Dr. Christoferson that this bill, as such, would probably not be introduced in the 1965 Legislature.

Dr. Ulmer spoke of the meeting the Committee on Legislation had held in March, 1963, when SB 320 was up for a vote in the House. Dr. Ulmer explained that it was learned at that time the Republican House members had refused to approve the Senate-passed transfer bill. He went on to say that the Legislative Committee was operating in a policy vacuum at that time. He and others urged the Delegates to give a broad and meaningful policy on the transfer of Institutions to the Committee on Legislation.

A substitute motion to Dr. Beithon's motion to approve the principles of SB 320 was offered by Dr. Ulmer. It was moved that the House of Delegates go on record in advising the Legislative Committee to support legislation which would improve the quality of care in the various State Institutions. Carried.

As the outgrowth of Dr. Pederson's earlier remarks in which he stated that Dr. Willard Wright was a candidate for President-Elect of the AMA, Dr. Painter moved that the House approve Dr. Wright's candidacy. Carried unanimously.

The following Resolution, introduced by Dr. Giltner for the Second District, was presented to the House and passed.

RESOLUTION

WHEREAS, the First District Medical Society staffed and supplied a first-aid station during the National Plowing Contest at the Fraase farm in September, and;

WHEREAS, the Lake Region District Medical Society commends the First District for its outstanding public service,

THEREFORE, BE IT RESOLVED that the North Dakota State Medical Association expresses its appreciation to the First District Medical Society for its excellent work in handling the first-aid station project at "Plowville, U.S.A."

The following Resolution was introduced by Dr. Hankins for the Ninth District, but withdrawn when it was noted the intent of the Resolution had been approved through House endorsement of the addition to the present District Health Unit Law.

RESOLUTION

1. WHEREAS: The Five District Health Units, serving 29 counties, meet an essential need in the Public Health field in North Dakota.

2. WHEREAS: The monies derived from a local three-fourth mill levy and matching state funds ($5 local and $1 state) are not sufficient to allow these units to fully carry out the duties assigned to them.

3. BE IT THEREFORE RESOLVED: That the North Dakota State Medical Association support permissive legislation for an increased mill levy in those counties served by the District Health Units for the support of these units.

Doctor Beithon, speaking for the Committee on Aging and Rehabilitation reminded the House that efforts to obtain greater utilization of the Medical Center Rehabilitation Unit was one of the committee's projects. He reminded the members of the rehabilitation facility, and asked them to consider its use.

As the final order of new business, Dr. Powers moved that the Association's booklet titled "The Positive Program of Health Legislation—1963" be revised for distribution in 1965. Seconded by Dr. Tudor and carried.

The House was duly adjourned at 3:25 P.M.

REPORT OF THE EXECUTIVE SECRETARY

GENERAL COMMENTS: Your Executive Secretary attended several State, Regional and National Meetings in behalf of the Association.

This year we celebrate the 78th birthday of the Association. Your Executive Secretary began his 14th year as of February 18, 1965.

Mrs. Margaret Fremming, Office Secretary, began her 15th year with the Association.

Mr. Daniel E. Buchanan, Director of Communications, came to us on October 1, 1961, and is showing steady progress.

Mrs. Myrtle Kohler, office assistant, joined us in March, 1962.

The routine of the Headquarters Office continued to show an increased tempo as each year passes. This increase is due to increased emphasis in the areas of Medical Economics, Legislation, Medicare, Public Relations, State Board of Medical Examiners duties and general services to the members.

LEGISLATION: Our greatest effort in this area was on the state level during January, February and March of this year. It was difficult to lobby in the House of Representatives during the 39th Legislative Assembly since there were so many new and inexperienced members present. The Association's positive legislative program was quite successful except in the attempt to improve on a present Kerr-Mills Law. We had introduced in the Senate, S.B. 119 (Medical Center Student Loan Fund), SB. 131 (Privileged Communication) and S.B. 277 (MAA Amendments). These were supported by the Association and with the exception of S.B. 277 passed and signed by the Governor. The Association supported H.B. 596 (Cancer Quackery Amendment to Include Dentists) which the Governor signed. Please note the report from the Committee on Legislation for the complete listing of legislation followed during this past session. The members of this Association who visited the Legislative Assembly and contacted their Senators and Representatives are to be commended for their efforts.

The 39th Legislative Assembly was fortunate in having amongst its membership a doctor of medicine, Senator James H. Mahoney of Devils Lake, who is a member of this Association. Dr. Mahoney was very helpful to this writer in his lobbying activities and was a co-sponsor of the three Senate Bills that our House of Delegates wanted introduced.

On the national scene, the war against the nationalization of medicine continues at a definitely stepped-up pace. At this writing (April 5, 1965) the House Rules Committee is expected to take up H.R. 6675, the Social Security Amendments of 1965. The House is scheduled to begin debate of the bill and take a vote on it later this week. It is thought that H.R. 6675 will be debated

by the House under a "closed rule" permitting no amendments from the floor. In its minority report, GOP members of the House Ways and Means Committee charged that this bill would cripple the Social Security System by loading it with staggering debts. Their minority report stated that the plan would impose on today's workers a $35 billion liability for hospitalization benefits for persons now over age 65. Following the House action, the bill will be sent to the Senate for consideration by the Senate Finance Committee. It is expected that this Committee will hold thorough public hearings.

PUBLIC RELATIONS: Mr. Daniel E. Buchanan has been assigned to this area of the Association's operations. It is this writer's opinion that slow but sure progress is being made in this field of our endeavors. Mr. Buchanan is to be commended for his work in up-dating the Association's pamphlet entitled "The Positive Program of Health Legislation." Please note the report of the Committee on Public Relations for more detailed reporting.

The Emergency First Aid Station, started in the 1963 legislative session, was again maintained during the 1965 session by the Association. This is a good public relations gesture but improvements in manning the station are definitely needed.

Our relationship with Blue Shield continues to remain strong in the area of public information and education.

PHYSICIAN'S PLACEMENT SERVICE: This office continues to give service to communities and/or medical groups seeking physicians.

U.N.D. MEDICAL SCHOOL SCHOLARSHIPS: The 1964 winners of the Association's Scholarship prizes (Totaling $500.00) offered at the School of Medicine were as follows:

Highest Average Mark in Physiology-Pharmacology—
John H. Bond, Jr., Fargo, N.D.
Highest Average Mark in Microbiology—
John H. Bond, Jr., Fargo, N.D.
Highest Average Mark in Pathology—
John H. Bond, Jr., Fargo, N.D.
Higest Average Mark in Anatomy—
Wayne A. Lattin, Power, Montana
Highest Average in the Work of the First Year—
Jerry R. Hordinsky, Drake, N.D.

FINANCE: The Treasurer's report continues to show an improved balance. The goal of having one year's operating budget in reserve was maintained last year when you consider the certificates of deposit in the Headquarter's Office account. It is hoped that this reserve can be kept at this level, as it should be, in the interests of good business practice.

Receipt of dues picked up a little this year.

MEDICARE: The Dependents' Medical Care Program (Medicare) commenced on December 7, 1956. Up to January 1, 1965, 10,951 claims had been processed by this office.

The total sum paid to North Dakota physicians as of December 31, 1964, amounted to $903,035.00.

Each claim for services rendered averages out at $82.46.

THOUGHTS FOR THE FUTURE:

1. Greater interest must be shown in the Legislative Assembly which convenes in Bismarck every two years. This interest can best be evidenced by members coming to Bismarck to visit their legislators, to testify before committees and to man the emergency first aid station.

2. The Committee on Medical Economics should initiate a review of all of the Association's fee schedule agreements (or contracts) with other agencies.

3. In our public relations program, personal contacts with persons and groups outside of medicine must be made and maintained.

ACKNOWLEDGEMENTS: Your Executive Secretary wishes to express his sincere appreciation to our President, G. Alfred Dodds, M.D., for his efforts in behalf of this Association. Dr. Dodd made many trips both in and out of the state on Association business.

I wish to also acknowledge the efforts of W. M. Buckingham, M.D. who is Secretary of the North Dakota State Medical Association and Vice-Chairman of the Committee on Legislation, for his whole-hearted cooperation during the 39th Legislative Session in testifying before committees and manning the first aid station.

My sincere thanks also go to the members of the Johnson Clinic in Rugby for manning the first aid station. Each member was "doctor of the day" during the past legislative session.

My sincere thanks also go to those other members with whom this writer has had occasion to work this past year on committee assignments and the several other programs of the Association.

Respectfully submitted,
(Signed) LYLE A. LIMOND, *Executive Secretary*

REPORT OF THE CHAIRMAN OF THE COUNCIL

The First Session of the Council was held Saturday, May 2, 1964 in Minot. The meeting was called to order at 10:00 A.M. by Dr. G. W. Toomey. The Secretary, Dr. C. H. Peters, called the roll and the following Councillors responded:

Drs. Frank DeCesare, Ralph Mahowald, R. W. McLean, Frank Naegeli, Tom Pederson, Dean Strinden, G. Christianson, Keith Foster and E. J. Larson, Councillor-at-Large.

Others present were: Drs. E. H. Boerth, R. D. Nierling, G. A. Dodds, Amos Gilsdorf, Lee Christoferson, R. C. Painter, Wm. Buckingham, and Lyle Limond and Daniel Buchanan.

It was moved by Dr. McLean, seconded by Dr. Foster, that the minutes of the previous meetings be accepted as printed in the Council Agenda. Motion passed.

Mr. Limond advised the Council that the budget had been accepted in December, 1963, at the Interim Meeting. However, it appears that there might be a shortage, or deficit, of $2,390.00. Mimeographed copies were passed out to the Councillors listing several solutions to the problem, entitled "Comments Regarding the Financial Status of the Association." Dr. Peters advised that he felt sure the potential membership dues would be in and would take care of this shortage.

Dr. Evans of Grand Forks appeared before the Council regarding the Rehabilitation Center at Grand Forks. The center has 41 beds and at the present time only twelve are being utilized. There is available the help of specialists for rehabilitating the injured, disabled and crippled and Dr. Evans asked the doctors for their support by sending patients to the Center for rehabilitation. He also asked that they visit the display that Miss Landon will have at the Exhibit Hall during this annual session. The Councillors asked Dr. Evans to appear before the House of Delegates with his message regarding the Rehabilitation Center.

Drs. Peters and Pederson explained to the Councillors, the Speaker's Bureau which they had attended. This is

a day and a half meeting put on by the American Medical Association, with professional speech instructors furnished for the physicians. Smith Kline & French provide the speaker's service without cost to medical associations and other groups interested in formulating a nucleus of speakers. Both doctors are of the opinion that there should at some time be a speaker's meeting such as this, held for at least twenty or more members of the Association, with the Woman's Auxiliary to be included. Dr. Foster made a motion that this speaker's meeting be implemented as soon as feasible through the Public Relations Committee. Dr. Naegeli seconded the motion and the motion passed.

Dr. Ulmer appeared before the Council with his message on AMPAC and COMPACT. After a general discussion, it was decided to ask Dr. Ulmer to appear before the House of Delegates meeting to deliver his message on COMPACT.

A motion was made by Dr. Peters, seconded by Dr. Pederson, that the medical students of the University of North Dakota be invited to attend the Interim Session of the Council and House of Delegates in Fargo in December, 1964. Motion passed.

Dr. Peters, as Chairman of the Committee on Constitution and By-Laws, asked that the Council approve of the revision, and request that the House of Delegates authorize the Committee to revise our present Constitution and By-Laws.

There was a general discussion on the election of Councillors. Dr. Christoferson advised that he would instruct the House of Delegates at the First Session regarding the election of officers as set forth in the By-Laws, Chapter V, Section 3, which states, "Nothing in this chapter shall be construed to prevent additional nominations by members of the House of Delegates for offices in the Association."

The matter of a change in the committee system to a commission system was discussed. It was decided that this would have to be worked out in detail and information mailed to the District Societies explaining the change. If the Constitution and By-Laws are to be revised, the commission system could be well outlined for study by that committee. Dr. Peters moved that the Council recommend to the House of Delegates that a committee be appointed by the President to begin a revision of the Constitution and By-Laws within the next year or two. Dr. Foster seconded the motion and motion passed.

Dr. Foster brought up an item of interest to all members, to be considered; namely, changing the system of meeting dates for the annual session so that the business sessions and the scientific sessions could be on the same day. For example, a business session in the morning, and a scientific session in the afternoon, thereby allowing many more doctors to attend both the business and scientific sessions. This was discussed at length and Dr. Strinden moved that Dr. Foster present a resolution to the House of Delegates, to amend the Constitution and By-Laws to allow for the annual meeting on Friday, Saturday and Sunday, with the recommendation that the House of Delegates give favorable acceptance to this resolution. Dr. DeCesare seconded the motion, and motion passed.

Mr. Limond discussed the item on the agenda of legislative "Key" men in District Societies. Dr. Peters moved that Mr. Limond draw up a resolution to be presented to the Committee on Resolutions of the House, asking them to instruct the District Medical Societies to appoint a legislative committee and legislative "Key" men for each county in the society, and coordinate their efforts with the Committee on Legislation. Dr. G. Christianson seconded the motion, and motion passed.

Mr. Limond asked that the Council authorize two men to attend a meeting with the Army Colonel on renegotiating the Medicare contract; such as Dr. Peters and the present Chairman of the Committee on Medical Economics, Dr. M. E. Nugent. Dr. Mahowald moved that Dr. Peters and Dr. Nugent be appointed to attend the meeting on Medicare, re-negotiation of the contract. Dr. DeCesare suggested that the President of the Association be allowed to name anyone else that he sees fit to go besides the aforementioned doctors. Dr. Mahowald added this to his motion. Dr. DeCesare seconded the motion and motion passed.

The meeting was recessed at 12:00 noon, to reconvene at 1:30 P.M.

Dr. G. W. Toomey, Chairman of the Council, reconvened the meeting at 1:30 P.M.

Dr. Gilsdorf made a few brief comments on the Cornell University Automotive Crash Injury Research. He advised that these people would like to continue this project for another fourteen months and he feels this is a worthwhile project. Dr. McLean moved that we go along with them and continue to furnish reports for this research program. Dr. Pederson seconded the motion and motion passed.

Dr. Gilsdorf asked that some thought be given to a solution to expedite the matter of resolutions presented to the House.

Dr. Gilsdorf also advised the Council that the Woman's Auxiliary has asked for advice from them regarding the dispensation of their Student Loan Fund; that is, if the Woman's Auxiliary should give their student loan fund to the AMA-ERF Medical Education Loan Guarantee Program, or if they should go through the Federal Program of matching funds, under the Health Professions Educational Assistance Act of 1963. The Council discussed this thoroughly—the merits of the AMA-ERF Fund as compared to the Federal Subsidy matching formula. Dr. Foster moved that the Council ask Dr. Gilsdorf to communicate to the Woman's Auxiliary that it is the concensus of the Council that they avoid alliances with the Federal Loan Fund. Dr. McLean seconded the motion, and motion passed.

Dr. Gilsdorf stated that he had received a letter from the Tollefson Group Life Insurance Agency asking for permission to canvass the membership. Dr. Gilsdorf informed the Agency that the Association would not object, but that neither the Council nor the House of Delegates would give preference to any agency in these matters.

A letter from Dr. John Swenson, Chairman of the Public Relations Committee, was then discussed. It was decided that the AMA Caravan, suggested in this letter, was a very good idea. Dr. Peters moved that the Council go on record as adopting the recommendations of Dr. Swenson and that the Chairman of the Council make the necessary arrangements to implement these recommendations; also that he write a letter to Dr. Swenson commending him for his excellent efforts in a very difficult field. Dr. Foster seconded the motion, and motion passed.

Dr. Christoferson brought up the subject of the planned Tetanus Immunization Program, fostered by the American College of Surgeons throughout the United States. This would be a Tetanus Immunization week during which publicity would go out to news media encouraging people to go to their doctors to be immunized. Dr. Christoferson asked the opinion of the Council as to whether or not this would be worthwhile for the

American College of Surgeons to implement here in North Dakota, and whether or not a resolution should be put before the House of Delegates to go along with the implementation of this thing. Dr. Peters moved that the Council approve of this program. Dr. Naegeli seconded the motion. Motion passed.

Adjournment at 3:00 P.M.

SECOND SESSION

Sunday, May 3, 1964, Minot, North Dakota

Dr. G. W. Toomey, Chairman of the Council, called the meeting to order at 5:00 P.M. The following doctors responded to roll call: Drs. Dean Strinden, G. Christianson, Ralph Mahowald, Frank Naegeli, R. W. McLean, Keith Foster and C. H. Peters.

The first item on the agenda was a letter from R. D. Nierling, M.D., requesting a recommendation from the Council as to the revocation of Dr. DuMais' license. Dr. Foster moved that this request be tabled in regard to any action from the Council and that the matter be handled by the Board of Medical Examiners. Dr. Naegeli seconded the motion, and motion passed.

Dr. Peters presented a letter about a proposed TV series recently outlined by Dr. Wheeler of the New York County Medical Society. These series are public service programs for television in which acknowledged medical authorities discuss subjects such as "Smoking and Health," "Heart Disease," "Drug Addiction," "Medical Quackery," "Mental Illness," "Cancer," and "Alcoholism." The series entitled "Your Health" will consist of approximately 130—4½ minute films. A general discussion followed, and Dr. Mahowald moved that the Council instruct Mr. Limond to go ahead with this program. Dr. Christianson seconded the motion and motion passed.

Dr. Toomey called for election of officers. Dr. Christianson nominated Dr. Strinden for the office of Chairman of the Council. Dr. Strinden nominated Dr. Mahowald for the office of Chairman. Dr. Mahowald nominated Dr. Naegeli for this office. The election was by ballot, and Dr. Mahowald was elected to the office of Chairman.

Dr. Mahowald then took over his duties as Chairman. Dr. Strinden moved that the Council give a rising vote of thanks to Dr. Toomey for past services to the Council. Motion passed unanimously.

Dr. Mahowald called for the election of a Vice-Chairman. Dr. Peters nominated Dr. Strinden for the office of Vice-Chairman, and Dr. Foster moved that nominations cease and that a unanimous ballot be cast for Dr. Strinden as Vice-Chairman. Motion passed.

Dr. Peters nominated Dr. Keith Foster for the office of Secretary of the Council. Dr. McLean moved that nominations cease and that a unanimous ballot be cast for Dr. Foster as Secretary. Motion passed.

Dr. Foster nominated Dr. Christianson as the Blue Shield representative. Dr. Christianson was unanimously elected. He will serve along with Drs. Mahowald and Christoferson as representatives of the North Dakota State Medical Association.

Dr. Mahowald set the interim meeting of the Council for Saturday, December 12, 1964 at Fargo; a breakfast meeting of the Executive Board to be held at 8:00 A.M., prior to the Council meeting.

Dr. Strinden made a motion that the Secretary of the Council send a letter to Dr. Willard Wright expressing appreciation for his faithful and diligent performance of his duties as Chairman of the Council on Medical Service of the AMA, and the manner in which he has aided and promoted the North Dakota State Medical Association. Dr. Naegeli seconded the motion and motion passed.

There being no further business, the meeting was duly adjourned at 5:30 P.M.

INTERIM COUNCIL MEETING

Saturday, December 12, 1964, Fargo, North Dakota

Councillors present were: Drs. Ralph Mahowald, Chairman, Keith Foster, Dean Strinden, R. W. McLean, C. H. Peters, W. R. Fox, Frank DeCesare, F. D. Naegeli, John Van der Linde, G. Christianson, and Amos Gilsdorf. Others present were: Drs. G. A. Dodds, W. T. Powers, J. D. Craven, R. D. McBane, Lee Christoferson, T. E. Pederson, Glenn Toomey, Wm. Buckingham, R. C. Painter, James Moses, R. J. Ulmer, J. R. Amos, and Mr. William Daner, Lyle A. Limond and secretaries Margaret Fremming and Myrtle Kohler.

A quorum was declared present at 10:10 A.M., and the meeting called to order by the Chairman, Dr. Mahowald. The first order of business was a review of the 1964 budget and the various expenditures explained by Mr. Limond. He advised the Councillors that there would be no deficit at the end of 1964 and that a one-year "cushion" was still being maintained. This is comprised of bonds and various C.D.s. The Council was advised that the proposed 1965 budget (the same as 1964) had been studied and approved by the Executive Committee. Dr. DeCesare made the motion that in view of the fact that the finances of the Association were on a solvent basis that the 1965 budget, as presented, be approved. Seconded by Dr. Foster and carried.

Discussion followed concerning the action on the part of the various District Society Secretaries in an effort to expedite the early payment of dues. Notices are now being mailed out urging the members to pay their dues during the month of December.

The matter of a raise in dues was discussed to possibly go into effect January 1, 1966. This suggestion was made in view of the fact that in a legislative year, expenditures may be higher. If the dues were raised from $100.00 to $125.00, the income of the Association would be increased by $10,000 per year. The Councillors were asked to discuss this with their respective District Society members and a decision to be made at the May 1965 meeting. It was the feeling of several Councillors present that unless it was felt there would be a deficit in the budget, a dues increase should not be considered.

Dr. Buckingham suggested that possibly one-half of the annual dues payment could be charged prospective new members coming into the state in view of the many expenses incurred by them prior to licensure. The State Office was instructed to send a listing of prospective members in the various Districts to the respective Councillors.

Dr. Amos was next introduced and first reviewed a proposed State Radiation Act. This involves a survey of X-ray facilities in physicians' offices and in hospitals for possible corrective measures to be taken for the protection of personnel and patients. The proposed Act has not as yet been drawn up but will be in form for presentation within a short time. Dr. Amos requested that endorsement be given by the State Medical Association for a program of voluntary X-ray survey of X-ray facilities.

Dr. Peters made the motion that the Council go on record as approving the proposal in principle, subject to the bill as printed and amended and subject to the Committee on Legislation's decision on ultimate outcome of the bill. Seconded by Dr. Strinden and carried.

Dr. Amos next discussed the licensing of medical hospitals and other facilities and stated his feeeling was that there should be revisions in the licensing law for the possible inclusion of nursing homes, boarding care and personal home care. The Council was asked for their support of this proposal. No action taken by the Council.

A request for endorsement of Revision of the District Health Unit law was next reviewed by Dr. Amos. Considerable discussion followed concerning Section 23-14-04 regarding the appointments to the local district health unit and the proposed deletion of the sentence "one of whom shall be a physician, one a dentist, one a business or professional man, one a farmer and one a woman." It was Dr. Amos' feeling that if this sentence were to be left in, members of the various other professions would wish to be included on such a board. It was the feeling of the Councillors if the sentence were to be deleted the local units could be controlled by politicians with no control by a Medical Advisory Board. At this point Dr. Peters strongly emphasized his feeling that a Medical Advisory Council to work with the State Health Council is urgently needed.

The members of the Council advised Dr. Amos that it was their feeling that there shouldn't be a district health unit without a physician on it and he agreed to convey their decision. Dr. Peters moved that the Council give approval to the amending of Chapter 23-14-04 as long as such proposed amendment did not include the elimination of a physician from the District Health Unit Board.

The motion was seconded by Dr. Foster and carried.

House Bill No. 813 (as amended) concerning the establishment of community mental health service units was next reviewed. The Councillors were advised that the Committee on Mental Health had gone over the bill carefully and had voted to approve, with changes. It was the opinion of those present that the Council should go on record as agreeing with the bill in principle and that the Committee on Legislation should use their judgment as to the reading of the finalized bill as printed and amended.

Dr. Ulmer was next called upon to give a report on COMPACT and AMPAC. He reviewed the 1964 activities and reiterated that no money is allocated for county-level candidates—the present goal is the National House of Representatives. He made the request of the Council that a Board of Directors of COMPACT be appointed by the Medical Association with members on the Board from each District with representation from the Auxiliary and possibly from the dental profession, etc. Mr. Daner was consulted as to the legality of such an action and advised the Council that it is actually not legal to have the Association appoint members to such a Board.

Dr. Ulmer completed his report with his request that each of the Councillors talk to the members of their respective Districts to gain more interest in the program.

Dr. Strinden, representing the Committee on Mental Health, next discussed the proposed Transfer of Institutions Bill. It was believed that such a bill will be introduced to transfer the State Hospital, Grafton State School and the Sanatorium at San Haven to the Mental Health Authority, Public Health Department. The Committee on Mental Health had asked the Committee on Legislation to support, in principle, such a transfer, and asked the same support from the Council. Dr. Amos was called upon for more details concerning the transfer and he also requested support of such legislation.

Dr. Peters reiterated his recommendation for the appointment of a Medical Advisory Committee to the State Health Council to determine policy of a medical nature in State Institutions. Such a committee could be appointed by the State Health Department, with recommendations from the Council or by the Governor or State Health Council.

A brief discussion followed concerning the request made by Dr. Carbone to the Committee on Mental Health for support of a proposal to erect an Adolescent Center at the State Hospital. Dr. Peters reminded the Council that such a Center had long been approved by the Council and that in principle such a proposal should be approved.

The attention of the Council was next drawn to the Proposed Code of Cooperation as formulated and adopted by the Committee on Public Relations of the Association. Mr. Daner's opinion of the Code was requested and he stated that it appeared acceptable.

The proposed Code will now be given to the Hospital Association, news media, etc., for their acceptance. They will, in turn, draw up their own and eventually after a meeting of all agencies, one Code will be drafted that is acceptable to everyone.

Dr. Peters made the motion that the Code be accepted as now formulated and presented. Seconded by Dr. DeCesare and carried.

Dr. Painter, representing the Third District, discussed a letter which had previously been directed by them to the State Office, concerning earlier publication of annual meeting transactions in The Journal-Lancet. It was his opinion that this has now been taken care of since the transactions appeared in the September, October and November issues this year.

The next item on the Agenda was a Bill—for an Act to amend and reenact Section 15-52-10 of the North Dakota Century Code relating to loan conditions applicable to loans by the Medical Center Loan Fund Board. Mr. Limond reviewed the Bill, advising the Council that it had been approved by the Committee on Legislation and would be presented to the House of Delegates by Dr. Ulmer. Considerable discussion followed concerning the proposed addition to the Bill—"The term 'Practice' under the agreement and repayment provisions of this chapter includes employment in the State of North Dakota as a medical intern or resident, or by the University of North Dakota School of Medicine." There was a difference of thinking among the Councillors as to whether or not the term "resident" should remain in the Bill. The Bill was to be referred to the House of Delegates with no definite decision made by the Council.

Dr. Peters reminded the Chairmen of the various Committees that they should be prepared to discuss all legislation which would be proposed at the time of the meeting of the House of Delegates. At this particular special session of the House, it is their purpose to act as a reference committee of the whole on all legislation and would be open for discussion. Any member of the Medical Association is given an opportunity to speak.

Mr. Limond next reviewed current Kerr-Mills legislation. He advised the Council that the Committee on Legislation had gone on record as favoring the expansion of the Kerr-Mills Statute. A small sub-committee was appointed to meet and decide upon general guidelines to present to the House of Delegates on Sunday. The committee would consist of Drs. Powers, Moses, O. W. Johnson, B. J. Clayburgh and possibly Peters.

Recess for lunch: 1:00 P.M.

The Council reconvened at 2:15 P.M. and continued their discussion of the Kerr-Mills Statute. Dr. Powers reported for the sub-committee that their opinion was that a recommendation for expansion of the program be

presented to the House of Delegates; that applications be simplified and streamlined; and that possibly a solution could be found to make the program more acceptable to the patients who resent applying to the County Welfare Board for assistance.

Dr. Peters said he approved the recommendations of the subcommittee and stated he felt the income levels should be raised; that the Board should accept income tax returns as evidence of eligibility; and that some clause should be inserted so that an applicant not be penalized who doesn't have a homestead.

Dr. Mahowald stated that the Council would go on record that the Bill be forwarded to the House of Delegates without a recommendation, except that improvements should be implemented, and instructed the Committee on Legislation to see that this is presented with recommendation for improvement.

Mr. Limond next discussed the possibility of an Advisory Committee to the Public Welfare Board following recent discussions with Mr. Ovre. Dr. Dodds stated that he had also talked to Mr. Ovre and it was his feeling that the guidance of a group provided by the Medical Association would be welcomed. It was his feeling that more cooperation would be forthcoming through such a combined effort.

No particular recommendation on this point was asked by the Committee on Legislation, and no action was taken.

The next item on the agenda was the Battered Child Syndrome—A Bill for an Act relating to the protection of children. A report was brought to the Council that the Committee on Crippled Children had approved the bill in principle at their meeting. Considerable discussion concerning the Bill followed, particularly the use of the word "shall" which was felt to be a directive. Section 4—Immunity from Liability—was given approval. No action was taken by the Council on this Bill.

The next item to be discussed was the Privileged Communication Statute, 31-01-06. The proposed addition and deletion had been studied by the Committee on Legislation, they went on record to support the amended Bill, and asked the Council for approval.

Dr. DeCesare made the motion that the Bill be approved by the Council. Seconded by Dr. McLean and carried.

Mr. Paul Avery of Bankers Life Company was next introduced. It is his wish to introduce a Keogh Retirement Plan to the membership of the Association, but must have endorsement by the Council before a plan of this type may be set up. A representative of Bankers Life explained the plan to those present and answered questions asked by the various Councillors. Mr. Avery and Associates were then excused.

After some discussion, motion was made by Dr. Naegeli that the Council give permission to Bankers Life Company to circularize the plan to the membership of the Medical Association, but not limit other companies from doing the same. Motion seconded by Dr. DeCesare and carried.

Dr. Pederson, Delegate to the AMA, next addressed the Council on the topic "How Do We Tell the Story of 'Organized Medicine' to the students at the UND School of Medicine." He reported briefly on the actions taken at the recent meeting of the AMA, most important of which was the need for concerted effort against the proposed Medicare legislation. It was his feeling that there were too many young doctors of liberal philosophy today, and that medical schools could do more to teach the concept of unfettered medicine. He felt some type of training for medical students could be implemented—possibly by obtaining speakers, etc. It is hoped that the staff of the UND might be interested in closer association with the Medical Association and the AMA.

Dr. Mahowald read a letter from Dean Harwood in response to an invitation for the medical students to attend the meetings of the Council and the House of Delegates. Dean Harwood explained that examinations were being held at that time, but asked for a representative to appear before the students and discuss action taken. The Council was advised that Drs. Mahowald, Powers and McLean were all to appear before the students for discussions within the next few months. The students are also invited to the Quain & Ramstad Fall Clinical Conference in Bismarck for participation in that meeting. Dr. Peters made the motion that a letter be directed to Dean Harwood offering a panel to be set up for discussing organized medicine, with material possibly being obtained from the AMA. Motion was seconded by Dr. Foster and carried.

Dr. Pederson advised the Council that the name of Willard Wright, M.D. would be presented in June, 1965 for the office of President-Elect of the AMA. The Executive Committee of the Council had given approval for a letter of announcement which was mailed out in September to Officers and Delegates to the AMA. It was Dr. Pederson's feeling that this announcement had been well received. Dr. Peters made the motion that the candidacy of Willard Wright, M.D., be endorsed unanimously by the Council and that the House be requested to do likewise. Seconded by Dr. Naegeli and carried.

The Council next discussed a Bill—For an Act relating to the treatment or cure of cancer and providing a penalty. They were advised that representatives of the dental profession had appeared before the Committee on Legislation requesting inclusion of the words 'or dentist' in the Bill. The Committee on Legislation approved the addition of the words 'or dentist' added after the word 'physician' in Sections 2, 3 and 4 of the proposed Bill. The motion was made by Dr. McLean that the Council give approval to the Bill and send it to the House of Delegates for approval and advice. Seconded by Dr. Naegeli and carried.

The last item on the agenda was the discussion of Resolution No. 6—Key Man Resolution. The Councillors were advised that it was the opinion of the Committee on Legislation that the format followed in the past be continued in the coming Legislative Session; i.e., personal contacts, telephone calls, etc. The Committee suggested that Resolution No. 6 be brought to the attention of the Council with the recommendation that each District President appoint "key men" in their individual districts who may assist in this program through close personal contact with local legislative members.

It was the concensus of the Council that the Association follow through on the above recommendation.

Dr. Dodds, President of the Association, thanked those present for their attendance and interest.

The motion was made by Dr. Naegeli that the Interim Meeting of the Council adjourn. Adjournment at 4:20 P.M.

It is recognized by this Chairman that this report is lengthy in content, but is the actual working of the Council, and, as such, a required report to the members of the North Dakota State Medical Association. An additional meeting of the House of Delegates being scheduled, the Interim Council meeting required considerable additional activity and lengthy discussion for

presentation of a legislative program before that body for action and guidance in the direction of the various Committees' activities.

Respectfully submitted,
(Signed) R. E. MAHOWALD, M.D.
Chairman of the Council

REPORTS OF COUNCILLORS

First District

During the last fiscal year, March, 1964, through February, 1965, the First District Medical Society held eight meetings. These meetings were all held at the Oak Manor Motor Lodge in Fargo. The March meeting was held on March 31, 1964, and was called to order by the President, Warren Macaulay, M.D. Minutes of the last meeting were read and accepted.

A communication from Mr. Limond was read. This was in reply to a request from the First District seeking more information regarding the Kerr-Mills program in North Dakota. Mr. Limond stated that he would make a survey of the membership of the Association in order to determine their thoughts regarding this program.

A further announcement was made by Dr. Macaulay concerning the future meeting of the Medicine and Religion Committee. Also announced was that the North Dakota State Health Mobilization Training Course was to be held in Bismarck May 12 and 13. The Public Health Committee, it was learned, would publish a new immunization schedule. The second application of Dr. R. C. Gaebe was read. Following the third reading of the applications of Dr. Wesley Palmer and Dr. John McMahon, they were unanimously elected into the membership of the First District Medical Society.

Dr. Barnard reported for the Operation Home Town Committee. He noted that 47 members had paid their assessment at this time, and that both Clinics had sent fillers with their statements with information about the King-Anderson Bill. Dr. Ulmer reported on behalf of the Organization and By-Laws Committee. He stressed the value of incorporating the First District Medical Society and moved that $300.00 be set aside to pay for the expense of incorporating the Society. This was passed unanimously. He also reported that the Welfare Board had agreed to pay bills retroactive to the day of admission to the hospital for treatment and should there be any misunderstanding between the individual physician and the local welfare office, that this matter should be brought to the attention of Mr. Ovre at the State Welfare Office. He also gave a report on behalf of COMPACT and AMPAC. He stated that about 30% of the members of this Society had made contributions.

Dr. Ted Donat, at this point of the meeting, publicly thanked the First District Medical Society for their contribution which helped make possible the North Central Television Station. He moved that the Public Relations Committee be authorized to review and approve programs that could be made available for viewing on Channel 13. His motion was seconded and passed unanimously.

Dr. Myron Burger of the State Health Department spoke regarding the State Mental Health Program and answered questions from the floor concerning the financing and staffing of this program.

The scientific portion of the program consisted of a very interesting discourse entitled "Office Management of Common Anorectal Disorders." This paper was presented by Dr. Stanley Goldberg. The meeting was adjourned at approximately 9:45 P.M.

The next regular monthly meeting was held on April 28, 1964. Again the meeting was called to order by the President, Dr. W. L. Macaulay. The minutes of the last meeting were read and accepted.

Dr. Robert Gaebe was unanimously elected to membership following the third reading of his application. At this meeting, Dr. Melton requested that the Delegates to the State Meeting report at our regular monthly meeting in September relative to actions taken at the time of the state meeting. Dr. DeCesare reported for the Public Relations Committee and summarized their activities for the year. He stated that the Committee previews programs for Educational TV and this included the series entitled "Making of a Doctor" which will be presented in three installments on May 12, 19 and 26. No report from the Community Disaster Committee or the Mental Health Committee.

The members of the First District Medical Society were invited to attend the meeting of the American College of Surgeons (North Dakota Chapter) which was to be held on the third Saturday in September at the Town House. Several reports were presented at this meeting, one by Dr. Burt on behalf of the Medical Review Committee, one by Dr. Macaulay who reported for Dr. Lancaster on behalf of the American Medical Education Fund and Dr. Wenz reported on behalf of the Liaison Committee with the local Bar Association. He stated that this committee was trying to get a group of impartial judges to determine if suits should go to court and therefore avoid unnecessary newspaper publicity. Operation Home Town activities were being carried on by the Speakers Bureau. Dr. Ulmer reported on behalf of the Constitution and By-Laws Revision Committee. He read the Articles of Incorporation and moved that these be adopted. This motion was passed unanimously. He discussed portions of the new By-Laws and he moved that the Constitution and By-Laws be rescinded and replaced by the Articles of Incorporation. He proposed that the By-Laws be voted on at the next meeting and adopted at that time. He also moved to suspend the reading of the new By-Laws at this time. The motion was passed unanimously. A copy of the Articles of Incorporation was enclosed with the report and minutes. Dr. Wayne LeBien reported on behalf of the Public Health Committee. He stated that revised immunization schedules and revised rules of isolation and quarantine had been formulated. Copies would be sent from the health office.

The meeting was adjourned at approximately 10:15 P.M.

The First District Medical Society does not hold a meeting in May because that is the month of the State Medical Association meeting. Consequently, the next regular monthly meeting was held on September 22, 1964. The meeting was called to order by the President, Dr. Macaulay. The minutes of the previous meeting were read and approved following a correction offered by Dr. Ulmer.

The President reported on a meeting that he had attended of the North Dakota Association of Medical Assistants. He urged that there be more interest by the Society in the Community Disaster Program and the President also called to the attention of the members present that a new narcotic agent had been assigned to this area and urged that all rules be followed to the letter for the dispensing of narcotics. More information on this subject would be received by the members of the Society.

At this meeting, Dr. Walter Owens announced that Dakota Hospital would be admitting patients in No-

vember and that staff membership applications from the society members were requested. Copies of the By-Laws and application blanks could be obtained from the hospital Administrator. He also announced that the Darrow-Long Lecture was scheduled for the evening of October 10th at the Oak Manor Motor Lodge. It was moved and seconded that the Darrow-Long Lecture be held in conjunction with the First District Medical Society and this would serve as the Society's October meeting. This was passed unanimously. He further stated that a Saturday afternoon scientific session would be held at the Dakota Hospital in conjunction with an open house for the area physicians and on behalf of the Dakota Medical Foundation, Dr. Owens invited the members of the First District Medical Society to attend this meeting. Dr. Kohlmeyer at this time invited the members of the District Medical Society to attend the meeting of the Institute for Suicide. Said meeting would be held Sunday, October 18th at the Town House.

Membership applications for H. A. Ohrt, M.D., and Ronald Olin, M.D. were read for the first time. Dr. DeCesare, in reporting for the Public Relations Committee noted the medical activities that had occurred at Plowville. He thanked the members of the Society who participated as well as Mr. Buchanan for his public relations help. He also thanked Mr. Steve Pezalla and Mr. Don Eagles of Blue Shield for their help and cooperation. In addition to the physicians who participated, a number of local nurses as well as complete ambulance service were volunteered. St. Luke's Hospital donated supplies and equipment. He moved that the Secretary of the Society send a resolution of thanks and commendation to the people and organizations who assisted at the Plowville medical section. This motion was passed unanimously.

Dr. Landa, the Secretary, reported at this time that $700.00 in donations was received from the members of the Society to be used for Operation Home Town. Two hundred and fifty-four dollars of this sum had already been dispersed.

At this time, Dr. Dodds, President of the North Dakota State Medical Association, was introduced by Dr. Macaulay. He spoke briefly regarding some of the activities of the State Society. Upon completion of his remarks, Dr. Dodds presented Dr. T. E. Pederson of Jamestown who is the North Dakota representative to the AMA House of Delegates. Dr. Pederson presented a resume of the functions and activities of the AMA and the House of Delegates. He presented a plea of endorsement for Dr. W. A. Wright for President-Elect of the AMA. Dr. Wright was formerly a member of the AMA House of Delegates from the State of North Dakota. After this presentation, Mr. Lyle Limond was introduced by Dr. Macaulay. He presented the results of the questionnaire that he sent out to the physicians in the State regarding the Kerr-Mills program in North Dakota. The First District Medical Society had requested this survey. Mr. Limond then introduced Dan Buchanan who spoke regarding the advertising campaign which would be launched in behalf of the Health Opportunity Plan for the Elderly. It was suggested by Dr. Macaulay that the Operation Home Town Committee handle this program locally.

Following these reports, Dr. Henry Norum of Fargo, acting as spokesman for the delegates from the First District to the State Medical Association, discussed several points that were brought up at the last State Medical Meeting. One of the points mentioned was that the format of the State Meeting be changed. It was suggested that the meeting be held on Friday, Saturday and Sunday instead of the present Saturday, Sunday, Monday and Tuesday. A show of hands demonstrated that this suggestion was favorably received. It will be brought up at the Interim Meeting of the State Medical Society which will be held on December 12, in Fargo.

The next portion of the meeting was concerned with review of the new By-Laws. Some of the proposed changes in the new By-Laws dealt with matters such as an affirmative vote of two-thirds of the membership of the Society being necessary for election and/or reinstatement of a member. Also, the meeting date of the First District, instead of being held on the last Tuesday of the month, to be switched to the last Monday of the month. This to become effective in January. A further change consisted of whether or not the business meeting should precede the scientific portion of the meeting and it was decided that this may be left to the discretion of the presiding officer. It was moved by Dr. Ulmer that the new By-Laws be accepted and this was done so unanimously.

The meeting adjourned at 10:15 P.M.

The next regular monthly meeting was held on October 10, 1964. President, Dr. Macaulay, presided. Reading of the minutes of the last meeting was suspended and the program turned over to Dr. Owens, who acted as Chairman for the Darrow-Long Lecture. Dr. Owens introduced three former Darrow-Long lecturers who were guests at this meeting. They were Dr. Claude Beck, Professor of Surgery, Western Reserve Medical School; Dr. Arthur Curtis, Professor of Dermatology, University of Michigan Medical School; and Dr. Donald Cassels, Professor of Pediatrics, University of Chicago Medical School. The program was then turned over to Dr. Philip Hodes, Professor of Radiology, Jefferson Medical College, who delivered the annual Darrow-Long Lecture. The title of the paper was "The Lymphatic System, the Third Circulation."

The meeting was adjourned at 9:30 P.M.

The next regularly scheduled meeting was held on November 24, 1964. The meeting was called to order by the President, Dr. Macaulay. Minutes of the September and October meetings were read and approved.

Dr. Mack Traynor, Program Chairman, introduced Mr. Leslie Ovre, Executive Director of the Public Welfare Board of North Dakota. Mr. Ovre presented an informal talk on the problems of the State Welfare Board with specific emphasis on the medical aspects. A question and answer period followed the presentation. Several members of the First District Medical Society made comments.

Dr. Macaulay then introduced Dr. R. W. Henderson, the medical consultant for the Public Welfare Board of North Dakota. Dr. Henderson spoke briefly.

Membership applications were presented by the Secretary. Second readings of the application of Dr. Ronald Olin and Dr. H. A. Ohrt were presented. The application of Dr. Leon Bjerke was read for the first time. Dr. Macaulay then mentioned that in order to complete the organizational minutes of the First District Medical Society it would be necessary to officially establish a bank account and present a resolution for writing of the checks. A resolution was passed unanimously to establish such a bank account at the Merchants National Bank and to approve the treasurer for the signing of any checks that would be necessary to transact the business of the Society. Approval of the charter, election of directors and officers, and adoption of By-Laws was carried out at the previous meetings.

At this time, Dr. Macaulay appointed a nominating committee to include Dr. Howard Hall as Chairman, Dr. B. A. Mazur, and Dr. George Ivers. He also appointed an auditing committee consisting of Drs. Poindexter and Hawn. Dr. LeBien, Chairman of the Public Health Committee, advised the Society that efforts were being made to combine the city and county health organizations. Dr. Lawrence, health officer, spoke on behalf of this proposal and he moved the endorsement of legislation combining city and county boards of health. The motion was passed unanimously. A copy of the proposed bill was included with the minutes. Dr. Macaulay notified the members of the First District Medical Society that any resolutions concerning proposed legislation for the 1965 North Dakota Legislative Assembly be submitted to the Executive Secretary of the North Dakota State Medical Association.

The meeting adjourned at 9:55 P.M.

The next regular meeting was called on December 22, 1964 by the President, Dr. Macaulay. The minutes of the last meeting were read and approved. The third reading of the applications of Dr. Ronald Olin and Dr. H. A. Ohrt was given. Following the readings, both members were unanimously elected to membership. The application of Dr. Leon Bjerke was read for the second time and the application of Dr. Dale Kana was read for the first time.

The Treasurer's report was read. A copy of this was enclosed with the minutes. The Chairman of the Auditing Committee, Dr. Hawn, reported that the Treasurer's report was reviewed and his Committee approved the report. There was no old or new business. Dr. Howard Hall reported for the Nominating Committee. The following candidates were nominated: Dr. Joseph Schneider for President; Dr. Blaine Amidon for Vice-President; and Dr. Marshall Landa for Secretary-Treasurer. Dr. Pray was nominated for the Board of Censors, term to expire in 1967. The following Delegates to the State Convention were nominated: Drs. Norum, Poindexter, Burt, Kulland, Paul Beithon, Amidon and Ulmer. Alternates selected were Drs. Gillam, Goltz, Gaebe, Fercho, Wasemiller, Sessums and Landa. The slate of the Nominating Committee was unanimously approved. There being no other business the meeting adjourned at 8:30 P.M.

The next regular monthly meeting of the First District Medical Society was held on January 25, 1965. The meeting was called to order by the President, Dr. Schneider. The minutes of the last meeting were read and approved.

The application for membership of Dr. Leonard Levine was read for the first time and the application for membership of Dr. Kana was read for the second time. Following the third reading of the application of Dr. Bjerke, he was unanimously elected into membership of the First District Medical Society.

At this meeting Mr. Linus Hayden of the Red River Council of Boy Scouts was offered an opportunity to discuss the sponsoring of a medical explorer post by the First District Medical Society. The President appointed Dr. Norum as Chairman of a committee to explore this problem further.

The scientific portion of the program was then taken up and Dr. Robert Ivers introduced the speaker, Norman Goldstein, M.D. of the Department of Neurology of the Mayo Clinic. The subject of his discussion was Neuritis. His talk was followed by questions from the audience.

Dr. DeCesare presented the report as Councillor of the First District to the State Medical Society. He presented a review of the Interim Council meeting of the North Dakota State Medical Association which was held in Fargo on December 12, 1964. A report of this is incorporated with the minutes of this meeting. As Public Relations Chairman, he requested that as many physicians as possible attend the State Legislative session as house physicians. No reports were heard from the State Legislative Committee, Operation Home Town Committee, Blue Shield Committee or the Mental Health Committee. Mr. Dan Buchanan of the Office of the Executive Secretary of the State Medical Society reviewed legislation which was to be presented this year at the State Legislature.

The meeting adjourned at approximately 10:00 P.M.

The last regular meeting of the First District Medical Society of the fiscal year was held on February 22, 1965. The meeting was called to order by the President, Dr. Schneider.

The scientific portion of the program was carried out first. Dr. Traynor introduced Mr. Frank Brennan, the Director of the North Dakota Heart Association. He then introduced the speaker of the evening, Dr. Robert Eliot of the Cardiology Department of the University of Minnesota. His topic was "Recent Concepts in the Diagnosis and Treatment of Rheumatic Fever." A discussion followed the presentation.

In the business portion of the meeting, it was noted that Dr. Pray moved that the First District Medical Society sponsor a medical explorer post of the Boy Scouts of America and that Dr. Norum be appointed to work out the necessary details to bring this about. This motion was seconded by Dr. Magill and was approved by voice vote. Dr. Mazur then notified the Society of a series of programs concerned with mental health that were to be presented over KXGO radio free of charge. The expense of the publicity would be carried by the Auxiliary and the Mental Health Association. Dr. Kent Darrow moved to commend the Auxiliary for its efforts on behalf of mental health. The resolution was passed by voice vote. Dr. Mazur reviewed the problems of the Poison Control Center. He emphasized the fact that all calls regarding poison control problems were to be transferred to one of the pediatricians in this area. He further asked for approval to pay for membership dues in the Poison Control Center Association for a recent book devoted to this problem. A motion relative to Dr. Mazur's request was made by Dr. Pray and passed by voice vote. Dr. Dodds spoke briefly concerning legislation pertaining to medical problems that are now before the State Legislature.

The application for membership of Dr. Obert was read for the first time and the application of Dr. Leonard Levine was read for the second time. Following the third reading of the application of Dr. Kana, he was elected unanimously into membership of the First District Medical Society.

Dr. Lamb mentioned that the North Dakota Arthritic Foundation would partially offset the cost of home nursing care for arthritic patients. The public health nurse or Dr. Lawrence should be contacted for this care.

A copy of committee appointments for 1965 was incorporated with these minutes.

There being no further business, the meeting was adjourned at approximately 9:30 P.M.

Respectfully submitted,
(Signed) F. A. DeCesare, M.D., *Councillor*
First District

Second District

The Devils Lake District Medical Society held nine meetings during the fiscal year from March 5, 1964

through February 2, 1965. These meetings were held on the first Thursday of each month of the year except June, July and August. There was excellent attendance at every meeting especially considering the distances that a good number of the members had to drive. Several new members were added to the Society and everyone actively participated in the spirited discussions of political and business matters. Officers for the present year were elected in January and are listed as follows:

President
DR. C. ROBERT MILLER ..... Bottineau

Vice-President
DR. DAVID A. RINN ..... Cando

Secretary-Treasurer
DR. L. F. PINE ..... Devils Lake

Delegates
DR. G. A. HILTS ..... Cando
DR. C. G. JOHNSON ..... Rugby
DR. L. T. LONGMIRE ..... Devils Lake

Alternate Delegates
DR. R. D. McBANE ..... Devils Lake
A. NEUENSCHWANDER ..... Rolla

Censors
DR. D. G. McINTYRE ..... Rugby
DR. J. TERLECKI ..... Minnewaukan

March 5. Dr. Ross Willows, head of Obstetrics Department, St. Boniface Hospital, Winnipeg, discussed the "Hypertension in Pregnancy." A short business meeting was held. Letters of appreciation from St. Andrew's School of Nursing and the University School of Medicine regarding scholarships which we made available to them were read.

April 2. The pre-convention business meeting was held. Dr. Toomey gave a brief report suggesting that committes be established on: 1. Religion-Medicine, 2. Mental Health Planning Committee, 3. Operation Home Town. It was also moved that the District Society buy 2,000 emergency identification cards to be distributed to the physicians. Discussion took place regarding the contributions to the Medical Loan Fund at the University of North Dakota Medical School and also regarding the incorporation of medical groups.

May 14. Post-convention meeting was held. Communication regarding Community Health Week in October was read. Communications from our Legislators in Washington were read regarding the Corporation Bill, which was being held in Committee. The reports of the Delegates and Councillor were then submitted. Discussion took place regarding how we would allocate the $1,000, which was donated to the North Dakota Medical School for scholarships. North Dakota School of Medicine students were presented and introduced.

September 11. Dr. Mark Lane, Neurologist from the Neuropsychiatric Institute, Fargo, North Dakota, presented an interesting paper on "Headaches." Three new members were accepted into the Society; namely: Dr. Glasner, Rolla; Dr. Rinn, Cando; and Dr. Mattson of Rolla. Regular business meeting was held. The September 11 meeting was held at Milligan Manor, Lake Metigoshe with the Bottineau Clinic arranging for the meeting and serving the refreshments and an excellent dinner.

October 1. Dr. Paul Johnson, Quain and Ramstad Clinic, Bismarck, spoke on the "High School Athletic Injuries Particularly the Injuries of the Knee." His talk was well accepted by the group. Regular business meeting was held.

November 5. Mr. Les Ovre, Director of the Public Welfare Board, Bismarck, was a guest speaker and gave an interesting report on the financing of the various agencies and the Public Welfare Program and discussed other mutual problems. A business meeting was held and a motion made that the $1,000 which we had sent to the University for the Medical Loan Fund be made available with federal matching funds.

December 3. Business meeting was held and chiefly taking up matters which were to be discussed at the Interim Meeting of the House of Delegates and Council in Fargo. The wishes of the Society were noted to instruct the Delegates and Councillor.

January 7. Our President, Dr. Dodds, addressed the group and Lyle Limond, Executive Secretary of the North Dakota State Medical Association discussed contacting the County Legislators when necessary during the Legislative Session. The election of officers was held. Dr. Hilts gave an excellent report of the actions of the House of Delegates Interim Meeting, and the Councillor discussed the decisions of the Council. Discussion of the Kerr-Mills Program and other welfare programs was also brought out.

February 2. Speaker for the evening was Dr. Rose of the University of Nebraska discussing "Stress and Relationship to Coronary Heart Disease." Due to the inclement weather, no business meeting was held as very few of the out-of-town members were able to attend.

Respectfully submitted,
(Signed) W. R. Fox, M.D., *Councillor*
Second District

RESOLUTION

WHEREAS, the North Dakota State Medical Association provided an emergency room at the State Capitol during the 1963 and 1965 sessions of the Legislature; and,

WHEREAS, the emergency service at the Capitol required a physician in attendance each legislative day; and,

WHEREAS, the selection of physicians was done on a random basis, with confusion to the State's physicians and those responsible for filling the dates often resulting; therefore,

BE IT RESOLVED, that the Second District Medical Society is on record in requesting the North Dakota State Medical Association to establish a definite system for staffing the emergency room at the State Capitol during Legislative Assemblies; and,

BE IT FURTHER RESOLVED, that the staffing be allocated proportionately to each District Society, to determine its own coverage accordingly.

Respectfully submitted,
(Signed) R. Donald McBane, M.D.
Alternate Delegate
Second District Medical Society

Adopted March 4, 1965
Devils Lake, North Dakota

Third District

The Annual Report of the Third District Medical Society Councillor is presented as follows:

The May meeting of this Society was held May 21, 1964 with more than a quorum in attendance and called to order by President Frank Hill, M.D. Dr. Harold Evans discussed the Committee on Aging and Rehabilitation's efforts to encourage accreditation of nursing homes and the inspection of same for this purpose; his request was accepted for informational value. The next order of business was a discussion regarding medical care of the students at the University of North Dakota and possible solutions to provide continuity of medical services during the time the Student Health Service is not operational. Considerable discussion ensued with a final motion by B. J. Clayburgh, M.D. to table until September. This was passed.

The next order of business was the disposition of the Blood Bank Records as it is now to be discontinued. It was moved by Dr. Painter to leave these records in the custody of Dr. Obert (who is willing to accept this responsibility) and duly passed.

President Dr. Hill then discussed the question of contraceptive devices and medication, and the action of the Welfare Board in that these cannot be purchased with Welfare funds. A conclusion that these be used for "Obstetrical and Gynecological Disorders" was suggested, meeting with apppoval for presentation to the Welfare Board Director.

W. T. Powers, M.D. then presented a report of the Blue Shield Board activity at the State Meeting. Dr. Robert Painter summarized a report concerning the action of the House of Delegates, and Dr. Mahowald presented a brief report of the Council at the Annual State Meeting.

The Third District Medical Society met on October 15, 1964 for its regular monthly meeting.

The first order of business was a motion by Dr. John Sandmeyer that the Society recommend "Individual Societies select their own Councillors." Duly seconded and passed after considerable pro and con discussion. Under new business, Dr. Hill, President, brought up the question of a cash door prize for the North Dakota Nurse Anesthetists Association meeting to be held in Grand Forks on October 21-22. Duly passed in the sum of $15, on motion of Dr. Sandmeyer and seconded by Dr. Powers.

The Society voted to forward a check for $200 to the Reverend John A. Shew, President of the Greater Grand Forks Council on Alcoholic Problems, Incorporated, on motion of Dr. Vandergon and seconded by Dr. Sandmeyer.

Discussion followed the presentation of a letter from the Cancer Society by Dr. Wallace Nelson regarding a Pap Smear Campaign. Because a successful campaign had been held in this area before and the patients and their physicians are adequately aware of the problem, it was decided to forgo such a campaign, and Dr. Nelson was to communicate this information to Dr. Lund.

A discussion of the "Why Pay Twice" program was then pursued at the direction of Dr. Mahowald, and the Society agreed to sponsor this program, advancing the money for a newspaper ad to be reimbursed by the AMA. This was followed by a discussion of the Blue Shield Board meeting by Dr. Mahowald regarding the consolidation of plans C and D. Dr. Charles Porter discussed this question, and stated this would be unnecessary, unwise and unsound, with the request that the Blue Shield Board members be so informed—accepted and passed.

Next a discussion by Dr. Tarpley concerning local and area Medical Civil Defense and the necessity of the Society taking leadership of the program. Dr. Tarpley was appointed Chairman of the Disaster Planning Committee to be named later, and the Committee will formulate a detailed plan for consideration of the Society's membership at a later date.

The November meeting of the Third District Medical Society was held November 19, 1964 with members of the North Dakota Academy of General Practice and the Northeast Counties Drug Association. An interesting discussion of drug addiction and the Federal Narcotic Laws was presented by Mr. Charles J. Klick of Minneapolis, Acting District Supervisor of the Bureau of Narcotics.

Old business consisted of a legislative discussion by Dr. B. J. Clayburgh regarding the measures to come up in the Legislature in the forthcoming session. It was pointed out these bills, as proposed, would be considered by the Council and the House of Delegates in the Special Meeting to be held in December, in Fargo.

The membership of the Society was then tendered an invitation on behalf of the Academy of General Practice to attend the Scientific Session and evening dinner in the next two days.

The December meeting of the Third District Medical Society was held December 17, 1964. The speakers of the evening, Mr. Leslie O. Ovre and Dr. Robert W. Henderson, Medical Consultant of the North Dakota Public Welfare Board, were introduced by Dr. Campbell, Program Chairman. The address and discussion revolved around the problems of (and their solution) the State Welfare Board in the implementation of its program.

The first order of business presented was the possibility of a 24 hour Student Medical Service at the University of North Dakota. The Society is to appoint a Committee of 3 to 5 members to meet with Dr. Starcher, President of the University, should he desire to discuss this problem.

A nominating committee was then named by the President, Dr. Hill, with W. C. Dailey, M.D., as Chairman, to present a slate of Officers at the next meeting for the coming year.

Four applications for membership were read and approved. These were—Emil Stefanov, M.D., Grafton and Robert C. Eelkema, M.D., Grand Forks for full membership; Major D. B. Dees, Jr., and Captain Wm. Earle Riley of the Grand Forks Air Force Base to be Service Members.

Robert Painter, M.D. presented a report of the Interim Meeting of the House of Delegates, followed by a report of the Council meeting by Ralph Mahowald, M.D.

The January meeting of the Third District Medical Society was held on January 22, 1965 at the Red River Valley Room at the Student Center, University of North Dakota. Special guests were G. Alfred Dodds, M.D., President of the North Dakota State Medical Association Dr. George W. Starcher, President of the University of North Dakota; T. E. Pederson, M.D., Delegate to the AMA; and Dan Buchanan of the State Association. All of these guests talked to the group concerning the problems of medicine and the methods proposed to correct them.

Election of Officers was held from names presented by the Nominating Committee Chairman, Walter Dailey, M.D.

President ..... KENNETH HELENBOLT, M.D.
President-Elect ..... ROBERT C. PAINTER, M.D.
Vice-President ..... WILLIAM P. TEEVENS, M.D.
Secretary-Treasurer ..... WILLIAM T. POWERS, M.D.

Delegates
ROBERT C. PAINTER, M.D., JOHN SANDMEYER, M.D., GEORGE COUNTRYMAN, M.D., RICHARD LEIGH, M.D., KENNETH HELENBOLT, M.D., ROBERT DELANO, M.D.

Alternates
WALLACE NELSON, M.D., WILLIAM POWERS, M.D., WILLIAM TEEVENS, M.D., HAROLD EVANS, M.D., B. J. CLAYBURGH, M.D., THOMAS L. SCHAFER, M.D.

Board of Censors
RALPH LEIGH, M.D., THEODORE HARWOOD, M.D., ERNEST GRINNELL, M.D.

The Blue Shield Directors remained the same with Wallace W. Nelson, M.D. succeeding himself.

The group then toured the Ireland Research Laboratory under the direction of Dr. Cornatzer who explained its relationship to the Medical School.

The February meeting of the Third District Medical Society was held on February 18, 1965. The speaker of the evening was Mr. Robert Vaaler, Attorney-at-Law, who discussed "Internal Revenue Service and You."

The new President, Kenneth Helenbolt, M.D., presented the following names for membership: P. M.

Ocampo, M.D., Arvids Vitums, M.D., Janis F. Sulcs, M.D., Gary D. Cody, M.D., and James R. Stone, M.D.

The above were approved for membership on motion by John J. McLeod, M.D. and seconded by Keith Vandergon, M.D.

Committee Assignments were announced by the President and are as follows:

Standing:

Awards ..... Harold I. Tarpley, Jr., M.D.
Legislative and Public Relations ..... B. J. Clayburgh, M.D., Richard K. Helm, M.D., Wallace W. Nelson, M.D., Nicholas Kaluzniak, M.D., J. M. Muus, M.D., and Norman M. Helgason, M.D.
Program ..... John A. Lambie, M.D.
Medical Review and Executive ..... Kenneth S. Helenbolt, M.D., Robert C. Painter, M.D., William T. Powers, M.D., William P. Teevens, M.D.

Special:

Valley Home Medical Advisory Committee ... John H. Graham, M.D., Wallace W. Nelson, M.D., T. Q. Benson, M.D.
Audit ..... Harold W. Evans, M.D., John H. Graham, M.D., R. Douglas Doss, M.D.
Hospitality ..... Hamish Mann, M.D.
Committee on Committees .... Kenneth S. Helenbolt, M.D., William T. Powers, M.D., Frank A. Hill, M.D., William P. Keig, Jr., M.D., Ralph E. Mahowald, M.D., and Walter C. Dailey, M.D.

After a lengthy discussion, it was moved by R. E. Mahowald, M.D., and seconded by J. J. McLeod, M.D. that a committee of three, plus a chairman, be appointed by the President of the Society to meet with President Starcher, to discuss the University Student Health Service. Motion was carried.

Ralph E. Mahowald, M.D., then informed the membership of a disaster meeting which will be held in Grand Forks on March 14, 1965, sponsored by the State Health Department, in conjunction with the University Medical School. He extended an invitation to all members to attend this meeting.

Matter of announcements: A letter was received from the State Medical Society announcing that Cyril J. Glaspel, M.D. of Grafton will be eligible for a 50-Year award to be given at the meeting in May of 1965. A letter was then read from Blaine E. McLaughlin, M.D. announcing his plans for setting up the Mental Health Clinics and the Mental Health Association in Grand Forks, and announcing a meeting which would be held on March 16, 1965.

The Third District, as will be noted from above, had lengthy monthly meetings and the membership has shown a keen interest in local and statewide medical problems. Considerable discussion with appropriate action has been the keynote for this past year, and it is felt by this Councillor that good participation and attendance have furthered the activity of this group. There has also been a keen interest in the forthcoming State Meeting to be held in Grand Forks, May 1-4, 1965, which has been very well handled by Special Committees under hard-working Chairmen.

Respectfully submitted,
(Signed) RALPH E. MAHOWALD, M.D., *Councillor*
Third District

Fourth District

The number of active, paid-up members affiliated with this Society, as of April 1, 1965, is 57. Five honorary members are carried on the membership rolls.

No new physicians became affiliated with the Society during the year preceding April 1, 1965, nor did any physician terminate his membership with the Society or move away from the Society's membership area.

The officers of the Northwest District Medical Society for the year 1964-65 are the same as those who served during the previous year, namely:

President ..... GALE R. RICHARDSON, M.D.
Vice-President ..... GEORGE M. HART, M.D.
Secretary-Treasurer ..... BRIAN E. BRIGGS, M.D.

The following meetings were held since April 1, 1964:

In April, 1964, an interesting meeting was held at the Minot Country Club at which Dr. Al Samuelson presented, in considerable detail, the National Mental Health program. There was considerable discussion of this program and its implementation in the State of North Dakota.

In May, 1964, there was no meeting—due to the Annual Meeting, held in Minot.

In September, 1964, the Society met at the Clarence Parker Hotel and enjoyed the presentation of Mel Lange, Instructor of Mathematics at Minot State College. At this meeting, there was also an interesting discussion of the American Medical Association's educational program relating to the Kerr-Mills Bill and its implementation in North Dakota.

In October, 1964, the Society met at the Clarence Parker Hotel and listened to a presentation by two representatives of the State Welfare Department: Ernest Appel, District Representative, North Dakota State Welfare Department, and Estelle Krick, Ward County Director of the Welfare Department in that county. An interesting and prolonged discussion followed this presentation by these two capable speakers, which related to the MAA, OAA, and other State Welfare sponsored medical care plans.

In December, 1964, a joint meeting was held with the members' wives at the Minot Country Club. An additional feature of the meeting was a movie, sponsored by the American Medical Association, relating to the Kerr-Mills Bill.

In January, 1965, a joint meeting was held, at Gordon's Holiday Spot, in conjunction with the Ward County Bar Association. Among the speakers were Mr. K. S. Peterson, and Mr. Bruce VanSickle, representing the Bar Association, and Drs. M. D. Peterson and H. Kermott, representing the Medical Society. These presentations and the discussion which followed provided an interesting and informative evening.

In February, 1965, the meeting was sponsored by the North Dakota Heart Association, which provided the speaker—Dr. Kenneth Rose, University of Nebraska. The presentation related to atherosclerosis and stress. An appreciative audience listened to this interesting talk and the discussion which followed.

The Society met at Trinity Hospital and listened to a very interesting presentation, relating to various forms of viral encephalitis or encephalitis of viral origin, presented by Dr. T. Chin and Dr. Allen Rowe, both research workers at the U. S. Public Health Service Laboratory in Denver, Colorado.

Respectfully submitted,
(Signed) FRANK D. NAEGELI, M.D., *Councillor*
Fourth District

Fifth District

The Sheyenne Valley Medical Society held six dinner meetings during the fiscal year March, 1964, through February, 1965. The first meeting was held March 18, 1964. Myron W. Burger, Psychologist, State Department

of Mental Health, discussed "Mental Health Planning."

The program for our meeting on April 17, 1964 was provided by Dr. Frank Melton, Dermatologist, Dakota Clinic, Fargo, North Dakota. Dr. Melton presented a very informative lecture, with slides, on differential diagnosis and treatment of fungus infections.

No summer meetings were held.

The first fall meeting was held on September 16, 1964. Dr. G. A. Dodds, President of the North Dakota State Medical Association, spoke about AMA services, statewide program for immunization against tetanus, COMPACT-AMPAC, "Battered Child Syndrome" legislation. Guests were Lyle Limond and Dan Buchanan. Mr. Buchanan presented plans for Kerr-Mills advertisements in local newspapers and over radio stations.

On October 21, 1964, the speaker of the evening was Mr. Leslie Ovre of the State Welfare Office. He explained the various welfare programs, differentiating between them, after which a question and answer period followed. Also present was Dr. R. W. Henderson, Medical Consultant to the State Welfare Board. The Society sponsored Kerr-Mills ads in the Valley City Times Record in conjunction with the State Medical Association. The Society also sponsored spot announcements on Radio Station KOVC.

The January 1965 meeting was devoted to Society business and election of officers and delegates as follows:

President ..... C. J. KLEIN, M.D.
Vice-President ..... M. O. BERG, M.D.
Secretary-Treasurer ..... J. W. GOVEN, M.D.
Delegate ..... W. R. JENSEN, M.D.
Alternate ..... C. E. JENSEN, M.D.

The February meeting was held in conjunction with the Seventh District Society in Jamestown. The program was sponsored by the North Dakota Heart Association. The topic was "Current Surgical Treatment of Congenital Heart Disease and Rheumatic Heart Disease."

The Fifth District now has a total active membership of nine.

Respectfully submitted,
(Signed) G. CHRISTIANSON, M.D., *Councillor*
Fifth District

Sixth District

Since the last report to the State Medical Association, the following meetings were held by the Sixth District Medical Society.

April 21, 1964, a "Double Header" Meeting was held with speakers on mental health and alcoholism. Dr. A. F. Samuelson, of the State Psychiatric Clinic, discussed Public Law 88-156, which deals with maternal and child health and mental retardation, and Public Law 88-164, which deals with mental retardation and mental health community centers. Myron Burger, Ph.D., Division of Planning, Training and Evaluation, Mental Health Services, N.D. State Department of Health, discussed the mental health survey that was being carried out. The second portion of the program was presented by Mr. E. J. Conlin, Jr., and Mr. Bernard Larsen, who discussed the Heartview Foundation, a non-profit alcoholic treatment center, located at Mandan, North Dakota. Dr. Thomas Gibson and Dr. S. M. Milligan were accepted for membership in the Society by transfer from the Northwest District Medical Society.

The next meeting was held on October 13, 1964. Mr. Leslie Ovre, Director of the North Dakota State Welfare Department, was the principal speaker, assisted by Dr. R. W. Henderson, Medical Advisor to the Welfare Board. This consisted of a discussion of the Welfare Board's attitude toward medical care and medical expenses with some illustrative examples and statistics, followed by an interesting question and answer period which further illustrated the Department's philosophy and attitude towards medical care for those unable to provide for their own needs in all age groups. Dr. R. W. Fardal was accepted into membership as a transfer from the Minnesota Zumbro Valley Medical Society.

A panel discussion on Medico-Legal Problems was held on November 12, 1964, by the Sixth District Medical Society and the local Bar Association.

At our next meeting on December 8, 1964, Dr. G. Alfred Dodds of Fargo, North Dakota, President of the North Dakota State Medical Association, reviewed the essential features which he felt the Legislative Committee would be pursuing in the coming session of the State Legislature, namely, the Battered Child Bill, City-County Community Health Centers, and methods of implementing and extending Kerr-Mills Bill applications. He also, briefly, reviewed the recent meeting of the AMA House of Delegates and several points which they were stressing, including a nation-wide Tetanus Immunization Program. Dr. Donald Carlsen was accepted as a member and Dr. Delano Pfeifle was accepted into membership by transfer from the Zumbro Valley Medical Society. A Tetanus Immunization Committee was appointed.

The following officers were elected for the coming year:

President ..... RALPH VINJE, M.D.
Vice-President ..... PAUL KLOSTERMAN, M.D.
Secretary-Treasurer ..... J. B. FRANKEL, M.D.
Board of Censors ..... P. L. OWENS, M.D.
Term ending 1967
House of Delegates ..... P. O. DAHL, M.D.
Term ending 1967
House of Delegates ..... J. J. MOSES, M.D.
Term ending 1965
Alternate ..... RALPH DUNNIGAN, M.D.
Term ending 1965
Alternate ..... ARTHUR EWERT, M.D.
Term ending 1965
Alternate ..... W. D. WALDSCHMIDT, M.D.
Term ending 1965
Alternate ..... GRANDON TOLSTEDT, M.D.
Term ending 1965
Alternate ..... W. J. ORCHARD, M.D.
Term ending 1965
Alternate ..... P. ROY GREGWARE, M.D.
Term ending 1965
Board of Directors ..... JOSEPH CLEARY, M.D.
North Dakota Physicians Service
Board of Directors ..... M. J. E. JOHNSON, M.D.
North Dakota Physicians Service

At our next meeting, held on February 2, 1965, in conjunction with the Auxiliary of the Sixth District Medical Society, Dr. Robert S. Eliot of the Cardiovascular Section of the Department of Internal Medicine, University of Minnesota presented a discussion on current treatment of the effects of rheumatic valvular disease, particularly by surgical means. Dr. Eliot was sponsored by the North Dakota State Heart Association and well accepted by the audience. Dr. Dale Oien, Dr. Arthur VanVranken, Dr. W. F. Hook, Dr. E. D. Peterson and Dr. W. C. Riecks were accepted as members.

The next meeting of the Sixth District Medical Society was held on Wednesday, March 3, 1965. Following the dinner, the speaker of the evening, Sgt. John Wrona, of the Bismarck Police Department, gave an interesting discussion of his narcotic control course, which he undertook in Washington, sponsored in part by this Society. This was followed by a discussion of some of the problems which have been seen and which might arise in our area in the future as regards narcotic control and narcotic distribution. He also had an exhibit of various

narcotic materials and implements used to self-administer the narcotics by addicts, gathered from various sources. Dr. Gilberto Gonzalez was elected to membership in the Society.

Membership in the District is as follows: Active members, 82; Honorary members, 6; Retired members, 1; Limited basis, 1. We gained 10 new members. Dr. Agnes Stucke and Dr. G. R. Lipp passed away during the year.

Respectfully submitted,
(Signed) C. H. PETERS, *Councillor*
Sixth District

Seventh District

The Seventh District Medical Society has had nine dinner meetings since last reporting. Attendance has been satisfactory. This is the first report of the new Councillor from the Seventh District.

March 26. Sixteen members in attendance, 4 guests present. Several programs were discussed including that of the Medical Auxiliary in collecting drugs, the activities of the local Cancer Society in sponsoring Papanicolaou Smear Clinics, and an announcement of the ensuing State Meeting in Minot in May. The speaker of the evening was Dr. Donald Lamb of Fargo, a plastic surgeon, who discussed various aspects of plastic surgery.

April 16. This was a special meeting, with members and wives present. The program consisted of the Jamestown High School Debating Team who debated the question: Resolved that the Social Security benefits be revised to include complete medical care. The discussion was very interesting and informative.

May 7. This was a meeting very well attended, and included the 4 medical students who were preceptors here in the month of May. The program was a presentation by Dr. H. Curtis Wood, of Fort Washington, Pa., a former obstetrician, and now Medical Field Consultant for the Human Betterment Association for Voluntary Sterilization. His presentation was extremely interesting and there was much discussion and many questions after the formal presentation.

September 24. After the customary summer interval, the meeting on this day was highlighted by the presence of Dr. G. A. Dodds, President of the North Dakota State Medical Association. He was accompanied by Mr. Lyle Limond, Executive Secretary of the Association, and Mr. Daniel Buchanan, Public Relations Director. The feature of the evening was Dr. Dodds' address, following which Mr. Limond and Mr. Buchanan made brief remarks. Mr. Steve Pezalla, of Blue Shield, also spoke briefly about Blue Shield coverage. The meeting was concluded with a film on microbial sensitivity.

October 29. The meeting this day was well attended; several items of business were discussed, including a discussion of a self-administered Pap Smear program. Mr. Leslie Ovre, Executive Director of the State Public Welfare Board, was speaker for the evening. He was accompanied by Dr. Henderson, Medical Consultant for the State Welfare Board. There was considerable discussion of the presentation by the 2 speakers for the Welfare Board, and much information was obtained, both interesting and informative.

December 3. The speaker of this evening was Mr. Charles Klick, Assistant Supervisor of the Narcotics Division of the Treasury Department, Minneapolis, Minnesota. Mr. Klick spoke on the subject of drug addiction, drug addicts, and there were, of course, many questions and much discussion after his formal presentation.

January 7, 1965. This was the annual meeting, and election of officers was held. Elected to the Presidency was Dr. Roger Engberg; Vice-President, Dr. Eugene Bolliger; Secretary, Dr. R. D. Nierling; Delegates, Drs. Elsworth and Hieb; Alternate Delegates, Drs. Miles and Clement; Censors, Drs. Curtis, Woodward and Clement; the Blue Shield Board of Directors, Drs. Sorkness and Clement; and the Blue Shield Corporation members were to be Drs. Elsworth, Van der Linde, Sorkness, Clement, Hieb, Hogan, and Swenson. The financial report was given by Dr. Nierling, the balance as of December 31, 1964 being $808.14, plus $6,308.75 Polio Fund.

There has been much discussion of the status of this polio fund at many meetings up to and including the last one, and it has not yet been decided how best to use this money.

Dan Buchanan of the North Dakota State Medical Association, presented the list of membership of the North Dakota House and Senate for 1965. Two films were shown, "A Clinic of the Deaf," and "Political Aftermath of 1964."

February 1. The highlight of this meeting was the address by the guest speaker, Dr. Robert S. Eliot of the University of Minnesota. Dr. Eliot spoke on newer concepts in prevention and treatment of Rheumatic Heart Disease. This was an excellent presentation and evoked much discussion afterwards.

March 25. This meeting was highlighted by the presentation of one of our own members, Dr. Hubert Carbone, Superintendent of the Jamestown State Hospital, who spoke on depression. His presentation was eloquent and evoked much discussion and many questions.

On September 24, 2 new doctors were elected to membership in the Society. They were Dr. James Bishop of Jamestown, and Dr. W. A. Hill of Kulm. Members leaving the society in the past year include Dr. John Jestadt of Jamestown, Dr. Robert Nolan of Jamestown, and Dr. Klassen of LaMoure.

Respectfully submitted,
(Signed) JOHN M. VAN DER LINDE, M.D., *Councillor*
Seventh District

Eighth District

The Kotana Medical Society held the following meetings during the year of 1964:

On January 24, 1964, the members entertained their wives at a dinner meeting. Election of officers was held with Dr. Gordon Ellis being elected President; Dr. R. E. Wiederanders, Vice-President; and Dr. Jerome Olson as Secretary-Treasurer. Drs. Robert Olson and Jerome Olson were accepted as new members into the Society.

For the February 7th meeting, the program was provided by Dr. Eliot of the University of Minnesota who discussed the subject of rheumatic fever and rheumatic valvular disease.

During the May meeting, the local dentists and their wives were entertained with the program given by the American Cancer Society. Dr. Arnold Kremen of Minneapolis was the main speaker with Dr. Amos R. Gilsdorf also addressing the group. Drs. Eion Harvey, J. I. Gonzalez, and Chang Jun made applications to become new members at this time.

In June of 1964 the Kotana Society sponsored an immunization clinic for tetanus, diphtheria and smallpox vaccinations. About 2,000 persons received immunizations at this time.

There has been much political activity and interest in the past year by the members of the Society at the meetings as a group, by the physicians individually, and also in the community as a whole. The Society has served as a board to provide doctors as speakers at lay meetings

to speak on medical politics and provide other information.

Respectfully submitted,
(Signed) DEAN R. STRINDEN, M.D., *Councillor*
Eighth District

Ninth District

The Southwestern District Medical Society during the years 1964-1965 had a total of 4 meetings constituting the business and professional affairs of a Society.

The first of these was in April of 1964 and consisted of a program presented by Dr. Albert Samuelson and Mr. Myron Burger of the Mental Health Authority in the State Health Department. These gentlemen acquainted our Society with the present status of planning on a state level prior to the institution of District Mental Health Units throughout the State. The program was very well received and it is our hope that this will be the start in the institution of a Mental Health Center serving Southwestern North Dakota.

Our next meeting was held in the Fall of 1964 at the Ray Hotel on the 10th of October. Our guest speaker for this evening was a Mr. Klick, who is an enforcement agent for the Treasury Department, Bureau of Narcotics. I think he gave a very interesting and informative talk on a narcotic addiction problem that is present in the State of North Dakota.

Despite the first heavy snowfall of the long, hard and miserable winter, Dr. Dodds, our State President, fought his way across the State to be with us on the evening of November 14th for his visitation to our Society. Our 2 gentlemen from the State Welfare Department were also to be present at this meeting, but were unable to attend because of the storm. Dr. Dodds' report on the progress of the affairs in this Society was well received and greatly appreciated by the membership.

February 3rd, 1965, Dr. Robert Eliot from the University of Minnesota presented a paper on Rheumatic Heart Disease under the auspices of the North Dakota Heart Association. At this meeting our officers for the ensuing year were nominated and elected.

These include:

President ..... DR. W. C. HANEWALD
Vice-President ..... DR. PAUL AHLNESS
Secretary-Treasurer ..... DR. R. F. RAASCH
Corporation members
DRS. R. J. DUKART, R. E. HANKINS, K. G. FOSTER, A. R. GILSDORF and W. C. HANEWALD
Blue Shield Board ... DRS. A. R. GILSDORF, R. E. HANKINS
Delegates ..... DRS. W. E. HANEWALD, R. E. HANKINS
Alternate ..... DRS. R. F. GILLILAND, N. B. ORDAHL
Councillors
DRS. A. J. GUMPER, D. J. REICHERT, R. C. THOM

Respectfully submitted,
(Signed) KEITH G. FOSTER, M.D., *Councillor*
Ninth District

Tenth District

The Tenth District Medical Society held 4 regular dinner and business meetings during the past year. Our members have been active and have been faithful in attending various committee meetings of which they are members.

In carrying out the recommendations of the State Association, there have been several immunization clinics in cooperation with the Public Health nurses. Some members of our group continue to be active and help maintain rapport with the general public by giving talks to P.T.A. and Civic groups. There have been no transfers from our group in the past year. One new member, Dr. Michael Leckie, Cooperstown, North Dakota, paid his dues and is awaiting admission to our District Society at our next regular meeting.

Elections were held at our meeting, February 3, 1965, and are as follows:

President
DR. RONALD KLOSTER ..... Mayville
Vice-President
DR. DONALD BREEN ..... Hillsboro
Secretary-Treasurer
DR. R. W. McLEAN ..... Hillsboro
Censor, 3 years
DR. KARL OJA ..... Portland
Censor, 2 years
DR. JAMES LITTLE ..... Mayville
Censor, 1 year
DR. DONALD BREEN ..... Hillsboro
Delegate
DR. JAMES LITTLE ..... Mayville
Alternate Delegate
DR. H. A. LAFLEUR ..... Mayville

Respectfully submitted,
(Signed) R. W. MCLEAN, M.D., *Councillor*
Tenth District

STANDING COMMITTEES

Committee on Medical Education

The Committee on Medical Education held its annual meeting on November 21, 1964 in Grand Forks. Dr. R. J. Ulmer, of Fargo, Chairman, presided. At its previous meeting, in 1963, the Committee had taken action to suggest to the various specialty societies in the state that they might wish to cooperate with this Committee in combining their fall meetings to the extent that they would meet in the same city, and share speakers of interest with each other. This proposal was made to the Chairmen of the various Societies. However, the proposal was either misunderstood, or of no interest to them, so that no coordinated effort seems possible at this time.

The Committee next discussed the matter of funds being made available for medical and nursing student loans by the various District Medical Societies. They were specifically asked by the Second District Medical Society to express an opinion as to whether or not these funds should be made available for matching of Federal loans. After considerable discussion, the Committee decided to recommend that any of the District Societies with such funds to disperse be encouraged to exercise their own free choice in the use of these funds, and that the Committee did not feel that the State Medical Society should either encourage or discourage the use of these monies to match Federal Funds.

The Legislative Research Committee of the State Legislature had met in the Fall of 1964 and made a number of proposals which would do away with so-called dedicated funds and have all tax monies placed into the general fund of the state. It was noted that this would possibly have an adverse effect on the medical center. The Committee was made aware of the fact that the medical school is now approaching the time when the mill levy will produce insufficient income to meet the budget, and that some additional source of funds will need to be obtained even if the mill levy is retained. There seemed to be no ready solution to the problem at the time of the meeting, and it was deemed best to wait until the Legislature had met and acted. It was felt, though, that the Committee and the State Medical Association should make known to the Legislature its feeling that adequate financing of the medical center was of the utmost importance, and should the mill levy be abolished, adequate steps should be taken to assure the

continued support and development of the medical center.

The Committee also discussed the bill which had been drawn, but not introduced in the 1963 session of the Legislature, which would extend the forgiveness features of Medical Center Loans to interns, residents and junior staff men at the University Medical School. After considerable discussion, it was decided to recommend this legislation to the Legislative Committee and to the House of Delegates at their meeting in Fargo, in December. This was done, and the House of Delegates amended the proposal as introduced to the extent that this would apply only to interns, and might also apply to cities of up to 5,000 population. This bill was subsequently drawn and introduced into the Legislature and was acted upon favorably.

Dr. Clifford Peters from Bismarck was present at the meeting, and along with Dr. Harwood, outlined for the Committee a proposed University affiliated residency program which the Quain and Ramstad Clinic hoped to implement in the fields of internal medicine, surgery, and radiology. The proposed program would lead to the Master's Degree on completion, and would be administered by the Medical School. It was suggested that such a program would help to attract physicians to the State, and would also provide a source of recruitment of well trained physicians to locate here. Dr. Peters emphasized that though this proposal was being initiated by the Quain and Ramstad Clinic, all other groups were invited to participate in it. It was further suggested that should the University give its approval to this program the State Hospital and the VA Hospital in Fargo would also be approached as participants. The Committee noted the proposal as a matter of information but took no action other than to recommend that all interested parties be invited to a meeting to discuss the plan.

The meeting was concluded by hearing the report from Dean Harwood on the progress of the Medical School during the past year. He emphasized that he felt too few students from North Dakota were entering the field of medicine and appealed to the physicians of the State to help with a recruiting program.

Respectfully submitted,
(Signed) R. J. Ulmer, M.D., *Chairman*
Committee on Medical Education

Committee on Necrology and Medical History

After we come to mature years, there is nothing of which we are so vividly conscious as of the swiftness of time. Its brevity and littleness are the theme of poets, moralists and preachers. Yet there is nothing of which there is so much--nor day nor night, ocean nor sky, winter nor summer equal it. It is a perpetual flow from the inexhaustible fountains of eternity:—And we have no adequate conception of our earthly life until we think of it and live in it as a part of forever. NOW is eternity, and will be, tomorrow and next day, through the endless years of God. Stebbins

JACOB VAN HOUTEN, M.D.

Dr. Jacob Van Houten, 87, a doctor whose practice dated back to the Pioneer days in Barnes County, passed away on May 21, 1964, at a Valley City Hospital.

Dr. Van Houten was born December 18, 1876, in Waupun, Wisconsin and attended grade and high school there. His medical training was received at Northwestern Medical School, Chicago, where he received his medical degree in 1905.

He located in Valley City the same year and was recognized as one of the last "country doctors," practicing mostly in the horse and buggy era of Barnes County. He was given national recognition for the organization of immunization clinics in the County. He remained in active practice until his retirement in 1950, and continued to reside in Valley City. He was a member of the Congregational Church, one of the founders of a City and State bridge club, serving for a time as state president of the organization. He was a member of the Holstein Breeders Association since 1917, an active member of the Barnes County Wildlife Federation, charter member of the Valley City Elks Club, and had served as Barnes County health officer from 1931 until 1959. He was a member of the North Dakota State Medical Association for many years and was made a member of the 50-Year Club in 1955 and given an Honorary membership.

Dr. Van Houten was married to Florence Hallock at Faribault, Minnesota in 1905. She preceded him in death in 1938. He is survived by two daughters and one son.

J. J. KORWIN, M.D.

Dr. Justin J. Korwin died at his home in Williston on June 26, 1964. He was 65 years of age.

He was born in Chicago in 1899 and was educated there. His medical training was received at Loyola University, Chicago, where he received his degree in 1926. He practiced medicine in Chicago for several years before locating in Williston in 1939. He was specialist in EENT.

Dr. Korwin was a member of the St. Joseph's Catholic Church, Knights of Columbus, and a past-exalted ruler of the Williston Elks Lodge. He had been a member of the Medical Association since the time of his licensure in North Dakota and was also a member of the AMA.

He is survived by Mrs. Korwin and two sons.

H. J. MEUNIER, M.D.

Dr. Henry J. Meunier passed away September 6, 1964, at the Masonic Memorial Hospital, Minneapolis, after a short hospitalization. He was 81 years of age.

He was born at Leopold, Indiana, January 24, 1883, and the family moved to a farm near Tell City, Indiana about 1895 where he attended high school. After attending high school, he taught country school, and attended the University of Louisville every other year until graduation in 1910. He was admitted to practice in Kentucky in 1910, in Indiana in 1911 and in North Dakota in 1912, when he was employed at the State Hospital in Jamestown. In 1914 he bought the practice of Dr. Braasted of Oakes and he resided and practiced there until a short time before his death.

Dr. Meunier was a long-time member of the North Dakota State Medical Association and was made a member of the 50-Year Club and given Honorary membership in 1960.

He married the former Jessie Hattendorf, who was also a physician and employed at the State Hospital, Jamestown, where he met her, the marriage taking place in 1914. She survives him together with one daughter and two sons.

W. F. SIHLER, M.D.

Dr. William Frederick Sihler, 87, retired Devils Lake physician and surgeon, passed away October 17, 1964 in the hospital there after a short illness.

He was born in Norfolk County, Ontario on June 13, 1877. His medical training was received at McGill University College of Medicine, Toronto, Ontario where he received his degree in 1898. Following graduation he practiced for a time in the Grand Harbor community.

In 1900 he moved to Devils Lake where he practiced until retiring several years prior to his death.

Dr. Sihler was a Fellow in the American and International Colleges of Surgeons, and a member of the State Board of Medical Examiners for 22 years, serving under six governors. He was President of the North Dakota State Medical Association in 1928, became a member of the 50-Year Club in 1948, and given Honorary membership in 1949. He served as company surgeon for the Great Northern Railway for over 50 years, and also was a surgeon for the Soo Line Railway. In 1907 he began establishing a hospital in Devils Lake, and the hospital and nursing school opened in June 1908. In 1914 a new General Hospital and nurses' home was opened, and he practiced there for 40 years. Prior to the opening of the hospital, there were no graduate nurses in the Devils Lake area.

He was one of the founders of the Town and Country Club, founded in 1920, and he was elected its first president, serving in that capacity through 1945. He was also a member of the Episcopal Church, a Mason, charter member of Kem Temple of the Shrine, and a Jester; a life member of the Elks, and a member of the Odd Fellows and Woodmen lodges.

Dr. Sihler and Anna A. Matthewman of Ottawa were married on January 22, 1902. She preceded him in death in 1959. He is survived by a daughter and one grandson.

D. D. RUBBERT, M.D.

Dr. Duane Rubbert, 33, died in the crash of a light plane on November 1, 1964 near Verona, North Dakota. It was his second solo flight.

He was born in Minot, North Dakota, March 28, 1931. He graduated from high school at Wahpeton in 1949, took his premedical instruction at Yankton, S.D. College, attended the University of South Dakota Medical College and graduated from the University of Kansas Medical School in 1958. He interned at the Mercy Hospital in Des Moines, where he remained until entering the Air Force Medical Service in 1960.

Dr. Rubbert began practice at LaMoure on May 1, 1962, joining Dr. Klassen at the LaMoure Clinic. He was an active member of the Air Force Reserve at Fargo and had reached the decision to become a pilot to facilitate travel between his duties with the Reserve and his practice at LaMoure.

He is survived by his parents, one sister and a brother.

G. R. LIPP, M.D.

Dr. George R. Lipp, 72, retired Bismarck physician, died in a nursing home in that city on November 24, 1964. He had been in ill health for 2½ years.

He was born at Brandon, Wisconsin, November 5, 1888. He received his schooling there, graduating from Brandon High School and Oshkosh Normal pre-medical school. He was graduated from the University of Illinois Medical School in 1916. He moved to Bismarck shortly thereafter and associated with the Roan and Strauss Clinic until 1924, when he entered private practice. He retired in 1962.

Dr. Lipp was a veteran of World War I, a member of the American Legion, the Elks Lodge and the Sixth District Medical Society, which he had served as president. He was a long-time member of the North Dakota State Medical Association. In 1949 he served as president of the medical staff of St. Alexius Hospital.

On April 6, 1920 he married Frances Kelley in Bismarck, who survives him, as do one daughter and two sons.

AGNES STUCKE, M.D.

Dr. Agnes Stucke, 90, long-time Garrison resident, passed away December 13, 1964 in a Bismarck Hospital. Dr. Agnes, as she was affectionately known, observed her 90th birthday in the Garrison Memorial Hospital, but suffered a serious hip injury when she fell December 8.

She was born on November 2, 1874 in Chicago, Illinois. She attended the Women's Medical College of Pennsylvania, graduating in 1910. Shortly thereafter she married Dr. E. C. Stucke in Philadelphia and they practiced medicine in Minnesota and McVille, North Dakota before moving to Garrison in 1911, when her husband was attracted to the area because of the many German-speaking folk.

In October, 1963 she was recognized by the North Dakota State Medical Association for 50 years of medical practice and was given an Honorary membership. She was a long-time member of the State Health Board and had traveled extensively and studied abroad.

Dr. Stucke was preceded in death by her husband in 1955. Dr. E. C. Stucke was serving as a state senator from McLean County at the time of his death. Also preceding her in death was their only son.

Respectfully submitted,
(Signed) E. H. Boerth, M.D., *Chairman*
Committee on Necrology & Medical History

Committee on Legislation

The Committee on Legislation met at the time of the Interim Meeting at Fargo on December 12, 1964, and again on February 6, 1965 at Bismarck, during the Legislative Session, for the purpose of evaluation of several bills specifically earmarked by our Association to be supported, to be objected to, or to be followed with interest. This was done by our good and faithful Secretary, Mr. Lyle Limond, who was our representative at all times during the session of the recent Legislature. He followed the Legislative Session blow by blow insofar as various types of legislation were concerned, especially involving medicine as it now exists in the State. Following this report is a breakdown of bills that were followed, that were supported, and that were objected to. There would appear to have been some bills that we probably should have watched just a little closer than we did because we do not want to be earmarked by our current legislature, or any other legislatures, as being the type of individuals who will support medical legislation only, and disregard all other legislation. So it behooves us to follow with interest many other bills outside those that allude to medicine specifically.

Again I would like to call to the attention of the membership that we are not as well organized as we might be in order to contact membership quickly insofar as their legislators may be concerned, if need be, on a rather sudden basis. I suspect this could be worked out much better if an evaluation were taken of the Legislators after the election in November, and actually the lists were gone through carefully at the Interim Meeting, which is usually held along about the middle part of December. This will allow enough time so that the man in the home district can acquaint himself with the problems that are uppermost at the time, insofar as the Legislative Session will be concerned, and they may be able to object to this one way or the other on a personal basis. I believe this could be worked out very reasonably and equitably and make it much easier for the Executive Secretary and his office force to meet oncoming problems before a final deadline appears.

Again, we were faced by bills from both the Chiro-

practic and Osteopathic Associations and would indicate that there was a good deal of objection to both. The objection was carried on by Doctors of Medicine in committee meetings comparatively successfully.

To summarize, there has been increased activity by State and Local Societies insofar as the Legislative Committee and the Legislature is concerned. Organized medicine has taken an interest in local and national politics more than in the past through AMPAC and COMPACT and various other approaches. There is little question that there will be attempts on a National scale to include physicians within the fold of Social Security and increasing a segment of the national population within Social Security medical legislation through Medicare. Whether this will be as it is now presented is difficult to say at this time, but I suspect that there is little question about the fact that medicine is now at the final line of defense and what will happen we do not know for sure. I suspect that the Administration will get some form of a Medical Bill instituted within these States in this session. I wish to indicate that the doctors of medicine have given a great deal of support to the political scene, both Nationally and Statewise, rather successfully within the last year or two.

Respectfully submitted,
(Signed) O. W. Johnson, M.D., *Chairman*,
W. M. Buckingham, M.D., *Vice-Chairman*
Committee on Legislation

SENATE BILLS

Number

10 Appropriates $12.9 million for the Public Welfare Board. Followed with interest. Governor signed.

26 Appropriates $685,700 for the operation and maintenance of the State Health Department. Followed with interest. Governor signed.

67 Authorization for counties and cities to provide informational, counseling and referral services for alcoholic patients, with assistance from the State Commission on Alcoholism. Followed with interest. Indefinitely postponed in Senate.

87 Permits the establishment of mental health and retardation service units by cities, counties or other political subdivisions, with direction and assistance by the Mental Health and Retardation Division of the State Health Department. Supported in principle. Governor signed.

105 Requires seat belts in 1966 and subsequent models of automobiles. Followed with interest. Governor signed.

119 Amends Medical Center loan law by providing forgiveness of loans to interns and to physicians who practice in towns of 5000 persons or fewer. Introduced and supported by Association. Governor signed.

131 Up-dates present law by making any communication made to a physician in the course of professional employment a priviliged communication. Introduced and supported by the Association. Governor signed.

176 Makes several changes in the law governing the organization and financing of District Health Units. Supported in principle. Governor signed.

182 Adds State Health Officer to the membership of the State Safety Committee. Followed with interest. Governor signed.

193 Provided state scholarships for the study of chiropractic. Opposed. Indefinitely postponed in Senate.

201 Provides and regulates the manner of disposition of one's own body. Supported. Governor signed.

202 Institutes a program permitting the development and utilization of sources of ionizing radiation for peaceful purposes, authorizes governor to enter into agreements with the Atomic Energy Commission, provides for licensing of materials, and designates the State Health Department as the licensing and regulating agency. Supported. Governor signed.

212 Establishes basis of validity as evidence of chemical analysis such as tests of a person's blood, urine, breath, etc. Supported. Governor signed.

226 Provided for the dissolution of the Board of Administration and the transfer of institutions under its control to other agencies. Supported in principle. Killed in Senate.

268 Authority to place TB patients in private hospitals, and the transfer of certain patients at Grafton State School to San Haven. Followed with interest. Killed in Senate.

277 Amendments to State's Kerr-Mills (MAA) program. Designed to raise income limits and allowable cash assets. Introduced and vigorously supported by Association. This bill was heard in committee twice. After the first hearing, it was slated for indefinite postponement. The full Senate concurred in the report of the Social Welfare and Veterans Affairs Committee.

279 Provides for the licensing and operation of clinics for alcoholism and addiction. Supported. Governor signed.

299 Makes several changes in the law concerned with nurse preparation scholarship loans, while raising the amount available under such loans. Followed with interest. Governor signed.

310 Designed to allow an income tax exemption to persons who support and maintain the mentally retarded. Followed with interest. Withdrawn.

328 Pays expert witness fees in the amount of $50.00 per day for time expended in preparation for trial. Supported. Governor signed.

HOUSE BILLS

519 Appropriates $150,000 for State Psychiatric Clinic, Bismarck. Followed with interest. Governor signed.

539 The so-called "battered child" bill. This measure requires that physicians and others report cases of apparent child abuse, by a parent or other custodians, to the juvenile commissioner, state's attorney, or the director of the Public Welfare Board's Division of Child Welfare. It also provides immunity from liability for such action. Supported. Governor signed.

556 Amendments to the State's Chiropractic Licensing Act, among which was this group's use of the term "Chiropractic Physician." The bill was strongly opposed. Principal opposition was aimed at the use of the term "Chiropractic Physician," which was removed from the bill before it became law. Governor signed.

596 Amends the 1963 Cancer Quackery Law to permit dentists to diagnose and treat cancer. Introduced and supported by the Association. Governor signed.

721 Provided clarification of the powers and duties of the State Health Council. Followed with interest. Indefinitely postponed in House.

730 Provided that Health Insurance Policies include 60 days of coverage for psychiatric or alcoholic illness, or carry a notice that such a provision is not a part of the policy. Also applicable to policies providing less benefits for psychiatric or alcoholic illness than for other illnesses. Followed with interest. Indefinitely postponed in House.

796 Creates a "Good Samaritan Act" for care given by nurses in an emergency, or during time of natural or man-made disaster. Followed with interest. Governor signed.

811 Creates Governor's Council on Human Resources to coordinate efforts in the areas of aging, children and youth, and employment of the handicapped. Followed with interest. Governor signed.

868 Inclusion of the services of Podiatrists (Chiropodists) in Blue Shield. Vigorously opposed by Association and North Dakota Physicians Service. Indefinitely postponed in the House.

878 Provided an exemption from certain prohibitions regarding cancer cures, on the basis of religious worship, devotion and healing. Followed with interest. Indefinitely postponed in Senate.

901 Designed to give doctors of osteopathy full medical, surgical and drug privileges, under the authority of their own licensing board. Strongly opposed. Indefinitely postponed in House. (See also House Resolution 7).

924 This bill was designed to provide funds for the erection of an Adolescent Treatment Center at the State Hospital. The House agreed to allow part of the money, to be available when the balance could be obtained, through Hill-Burton Funds or other sources. Supported. Indefinitely postponed in Senate.

945 Transferred the administration and control of the State Hospital, Grafton State School, and San Haven TB Sanitorium from the Board of Administration to the State Health Department. Passed House, but lost in the Senate for lack of a two-thirds majority. Reconsidered in the Senate, and amended to transfer State Hospital only. Supported in principle. Governor signed State Hospital Transfer.

946 Authority to place TB patients in private hospitals. Followed with interest. Killed in Senate.

House Concurrent Resolution D-1—Directs the Legislative Research Committee (LRC) to study and review laws pertaining to the care and treatment of the mentally retarded. Followed with interest. Adopted.

House Resolution 7—Directs two members of the 39th Legislative Assembly, together with two members of the State Board of Medical Examiners, and two members of the State Board of Osteopathic Examiners to study the feasibility of a single licensing Board for physicians and osteopaths. Supported. Adopted.

Committee on Public Health

No formal meeting of the Public Health Committee has been held during the past year. However, it is planned to hold a meeting in Grand Forks on April 23, 1965 in conjunction with the meeting of the North Dakota Public Health Association.

However, at the last meeting of the Public Health Committee, the Committee offered to serve as an advisory Committee to the Safety Responsibility Division of the State Highway Department in Bismarck. On March 26, 1965 a meeting was held with members of the State Health Department, and two members of the Public Health Committee, Dr. W. M. Buckingham, and myself. Others present were: Dr. J. R. Amos, Mr. W. Van Heuvelen, Ken Mosser, J. York, Dan Buchanan, and Mr. Ferguson and Mr. Kucera of the Safety Responsibility Division of the State Highway Department. The latter two are responsible for the issuance of drivers licenses in the State of North Dakota.

A broad discussion was held on the question of issuing drivers licenses, particularly substandard licenses such as to diabetics, epileptics, alcoholics, psychotics, etc. What came out of this meeting, or what I think is the most important part, is the request from the Safety Responsibility Division for an Advisory Committee that could help them in deciding which persons should or should not be given drivers licenses when medical consultation is needed.

This is a broad subject and there has not been a great deal of research in the country on the effect of substandard drivers and over-age drivers driving cars.

However, it is felt that a beginning should be made to cut down on accidents on the highways. It is felt that this is a field which might bear fruit. The Chairman of this Committee was privileged to attend a meeting in Chicago of all the representatives of the licensing departments in the United States, at which time an address was given by Surgeon General Terry, stressing the importance of more attention to the field of drivers licenses and also more research in this field. It was generally felt that the States should have medical advisory committees who could help the Motor Vehicle Departments decide on the question of issuing licenses.

Respectfully submitted,
(Signed) Percy L. Owens, *Chairman*
Committee on Public Health

Committee on Public Relations

The Committee on Public Relations has again completed an active year.

Your Chairman, Vice-Chairman, State President, and headquarters staff attended the AMA Public Relations Institute in Chicago last August. The Institute affords an opportunity for frank discussion of areas in which our PR efforts can be improved, while giving helpful suggestions on ways to be more effective. The staff of AMA's Communications Division is to be congratulated for the high quality program presented.

1964 saw further steps taken toward the development of a Code of Cooperation among physicians, hospitals, and the news media. A revised draft of the Code was adopted by the Council in December. Our objective now is to meet with representatives of the hospital, press, and broadcasters associations for the purpose of developing a mutually-acceptable document. When a joint Code has been prepared, we will ask for adoption or amendment by the Association. Dr. R. E. Mahowald, and the members of the sub-committee who prepared the Code, are sincerely thanked for their hard work.

A Speech Training Seminar was conducted in Fargo on April 10-11. Its purpose was to review principles of effective speech delivery, speech organization, extemporaneous speaking, and the mechanics of operating a speakers bureau. Instruction was furnished by Smith Kline and French Laboratories, Philadelphia, through their Speech Training Service. It is felt that such training will prove its value many times over in our ongoing efforts to communicate with the public.

Last September during the National Plowing Contest, the First District Medical Society, under the capable direction of Dr. F. A. DeCesare, staffed an Emergenccy First Aid Station at the "Plowville, U.S.A." site. This project enabled Medicine to demonstrate its sincere interest in the health and safety of the large crowds in attendance. The medical profession also enjoyed excellent publicity through the press, radio and TV for this effort. In addition, many favorable comments were voiced for the service, particularly from those persons whom the station actually served.

Another activity encouraged by your Committee is the staffing of an emergency service at the Capitol during sessions of the legislature. It is hoped that this will be continued during subsequent legislative sessions, and that more physicians will offer to go to Bismarck for a day at the station, while visiting with their legislators.

A project begun by the Committee since our last report is an Orientation Kit for new members. Dr. P. B. Curtis is serving as Chairman of the sub-committee in charge of its development. Such a kit will serve as a guide to new physicians establishing practice in the State, and will give them information concerning the State Association, as well as the voluntary and governmental agencies with which they will come into contact.

It is sincerely hoped that Districts will continue to establish PR committees, to give the State Committee the local follow-through in various programs. Societies are also encouraged to pick a physician to serve as information officer, in order to provide liaison between the society and the communications media.

Again, we wish to encourage Districts and individual members to make continued use of the available PR aids such as pamphlets, posters, films, etc. These materials are readily available, and can usually be obtained from the State Office.

Our sincere appreciation to Dan Buchanan, Lyle Limond, Mrs. Fremming and Mrs. Kohler for their assistance during the year.

Respectfully submitted,
(Signed) John A. Swenson, M.D., *Chairman*
F. A. DeCesare, M.D., *Vice-Chairman*
Committee on Public Relations

Committee on Official Publication

There was no meeting of the Committee on Official Publication during the past year, and to my knowledge no business which needs consideration in the near future.

The Committee has been satisfied with the publication

situation as it exists, and plans no change in the near future.

Respectfully submittted,
(Signed) CHARLES B. PORTER, M.D., *Chairman*

Committee on Medical Economics

The Committee on Medical Economics has not held a meeting since March 21, 1964.

However, as proposed in the report of the Committee in May, 1964, Mr. Les Ovre, Executive Director of the Public Welfare Board, and Dr. R. W. Henderson, Medical Consultant for the Public Welfare Board, made visitations to eight of the District Medical Societies and explained many of the problems encountered in providing medical aid to the needy of our State. These visitations were informative and helpful. Certainly greater understanding has been achieved by these visitations in the problem areas of the Administration, vendors, and recipients in providing medical assistance to our needy.

The fourth edition of the California Relative Value Studies (August, 1964) has been received. It is planned to evaluate this new California Study with the possibility in mind of revising the North Dakota Relative Value Schedule as adopted in October, 1958, and revised in March, 1962.

Respectfully submitted,
(Signed) O. V. LINDELOW, M.D., *Chairman*
J. F. HOUGHTON, M.D., *Vice-Chairman*

Committee on Rural and School Health

There was no official meeting of the Committee on Rural and School Health during the past year.

No correspondence has been referred to this Committee for study. The Chairman of the Committee has made talks to P.T.A. and Civic groups on subjects involving school health and also on Mental Retardation.

The Chairman plans to again attend the National Meeting in Chicago on Schools and Physicians.

Respectfully submitted,
(Signed) R. W. MCLEAN, M.D., *Chairman*
Committee on Rural and School Health

SPECIAL COMMITTEES

Committee on Cancer

The Committee on Cancer had 2 formal meetings during the year 1964-65. Our first meeting was held in May, 1964, in conjunction with the State Medical Meeting in Minot. During 1963, we had decided to introduce a Cancer Quackery Bill in the State Legislature. We were happy to see our efforts rewarded by a passage without too much opposition. This Bill was amended this year to include the dentists in North Dakota.

Dr. John Elsworth briefly discussed a Pap Smear Clinic which he conducted in the Jamestown area in the spring of 1964. The people were notified by radio and newspapers that the month of April was designated as Cancer Month and were encouraged to see their local doctor for examination which included a Pap Smear and pelvic examination. It was the opinion of the Committee that we should exploit this procedure and attempt to institute similar clinics in the other medical districts. Following our meeting, a letter was sent to all members of the Cancer Committee suggesting that they consult with the local pathologists in an attempt to arrive at a reasonable method and a reasonable fee for examining Pap Smears.

Our next meeting was held in conjunction with the Interim Session in Fargo, December 10, 1964. At this time, letters from the Cancer Committee members were discussed. Various papers were read from the Committee members relative to my inquiry. The reports were not too encouraging as it appeared that the pathologists are tremendously overworked. It would place a severe burden on them to help us in our project. As we would be unable to carry out our project without the help of our pathologists, our plans were abandoned temporarily.

It was decided that we should individually appear before our district medical societies requesting a short space on the program to encourage cancer detection examinations during the month of April. These examinations should include a physical exam together with proctosigmoidoscopy, pap smear and chest X-ray. Further X-ray study should be at the discretion of the examiner.

North Dakota Division of the American Cancer Society continue their activity in North Dakota. An assistant State Director and a new field man have been added to the home office. Dr. O. W. Johnson, Rugby, North Dakota, is President of the North Dakota Division and also North Dakota delegate and member of the National Board of Directors of the American Cancer Society. Dr. John Gillam of Fargo is Chairman of the Executive Committee of the North Dakota Division.

We urge all of you to help these officers and your local county commanders in their efforts to promote cancer control in their cancer programs and drives in your area.

Respectfully submitted,
(Signed) CARROLL M. LUND, M.D., *Chairman*
Committee on Cancer

Committee on Nursing Education

Your Committee on Nursing Educaction held a joint meeting with the representatives of the North Dakota State Nurses Association on Saturday, November 28, 1964, at St. John's Hospital in Fargo, North Dakota. This meeting was in conjunction with a similar group from the State Nurses Association. Some of the gray areas discussed were venipuncture, intratracheal suction, external cardiac massage, administration of anesthesia during labor, vaginal examination, and pronouncement of death. It was the feeling of the Nurses Association that steps should be taken in the State to clarify the gray areas. Dr. Dodds, who attended the meeting, assured the joint committee that maximum cooperation between the medical and nursing professions should be sought here; however, he warned that any statement of principles in the areas of medical nursing practice would have to allow for individual differences from hospital to hospital and patient to patient. The Nurses Association proposed that, as the first step in the clarification of gray areas, a joint statement be adopted on venipuncture. Such a statement, as adopted in California, is summarized below:

A nurse may start and administer fluids intravenously in California, if all the following conditions exist . . .

1. The nurse has had special competent teaching in the technique.
2. The technique is performed upon the order of a doctor.
3. The order is for a specific patient.
4. Where the procedure is to be performed in a hospital or any organized agency, the procedure be performed within the frame-work of designated preparation and practice of the nurse established for the hospital or agency by a committee composed of representatives from the Medical Staff, the Department of Nursing, and the Administration. This frame-work of prepara-

tion and practice to be reproduced in writing and made available to the total Medical and Nursing Staffs.

5. It is the jurisdiction of that committee in a hospital or organized agency to—
   A. Decide if the nurses in the hospital or agency may perform the technique.
   B. Determine the special method of teaching to be required.
   C. Establish in-service teaching of the technique for any nurses who may not have had adequate previous instruction.
   D. Delineate the types of fluids or medications that nurses may administer intravenously.
   E. Determine whether physicians' orders should be written or oral.

After a good deal of discussion, it was decided by the Nurses Association to continue such discussions of gray areas with the Hospital Association with the hope of developing a statement of principles on venipuncture and possibly other areas by May of 1965 for submission to the Medical Association's House of Delegates.

Some time was also spent in discussing North Dakota's Good Samaritan Act. The Nurses Association would like to see it amended to include them and hoped the Medical Association would support them in such an endeavor.

Another meeting of this Committee is scheduled for March 20, 1965.

I think we are fortunate in probably getting a little better cooperation in this State from the Nurses Association than the physicians are getting in many of the other states.

Respectfully submitted,
(Signed) G. W. Toomey, M.D., *Chairman*
Committee on Nursing Education

Submitted by:
COMMITTEE ON NURSING EDUCATION

Proposed Joint Statement on the
Intravenous Administration of Fluids*

It is recognized that under controlled conditions in many parts of the State, licensed professional nurses have been administering fluids intravenously.

With the objective of protecting the patient, the doctor, the nurse, and the hospital, the North Dakota State Medical Association acknowledges its acceptance of the legal right of nurses to start and administer fluids intravenously if all the following conditions exist:

1. The nurse has had special instruction in the technique and has had her competency verified.
2. The nurse performs the technique upon the order of a licensed doctor of medicine for a specific patient.
3. In a hospital or any organized health agency, the procedure is to be performed within the frame-work of designated preparation and practice established for the hospital or agency by a committee composed of representatives from the medical staff, the department of nursing, and the administration. This frame-work of preparation and practice to be reproduced in writing and made available to the total medical and nursing staffs.
4. It is the jurisdiction of that committee in a hospital or organized agency to:
   A. Determine which nurses in the hospital or agency may perform the technique.
   B. Establish inservice teaching of the technique for all nurses, specifying methods of instruction and practice under supervision.
   C. Decide which types of intravenous fluids or medications may be administered by nurses.

*Intravenous administration of fluids is accepted as meaning the introduction of fluids and medications prepared for introduction into a vein.

Committee on Maternal and Child Welfare

The Maternal and Child Welfare Committee of the North Dakota State Medical Association met in Fargo on Saturday, September 12, 1964.

1. A discussion was held regarding the best use of funds from the National Foundation, to implement our Crippled Children's Services provided by the State. This is in lieu of setting up another birth defect center.

2. The State Health Department will do PKU determinations at the six weeks check-up of recent newborns of suspicious cases. The doctors will receive notification of the availability of this test through Dr. Alice Peterson and the State Health Department.

Respectfully submitted,
(Signed) Robert E. Lucy, M.D., *Chairman*
Committee on Maternal and Child Welfare

Committee on Foreign Trained Physicians

The intern shortage in the United States and the foreign graduate as an intern continues to be a problem for the Council on Medical Education of the AMA and for many hospital administrators. A heavy concentration of foreign graduates in a hospital may tend to produce staff indifference, and a satisfactory educational program in such hospitals may be lacking. This applies especially to the smaller hospitals and to those who have no medical school affiliation.

The abolition of temporary E.C.F.M.G. certificates was a constructive move, and this has been of assistance to State Boards of Medical Examiners.

The 84 medical schools in the United States graduated 7,336 physicians last year. There are 7,138 hospitals in the United States and 1423 of these have approved educational programs. There are 12,229 approved internships, but only 79% of these are filled; 7,264 with U.S. medical graduates and 2,372 with foreign medical graduates.

Last year, 2,781 foreign graduates were examined by State Boards in the United States, and of these, 1,861 passed. This represents a failure rate of 33% plus. Foreign graduates are not licensed in Arkansas, Louisiana, Oklahoma, and Nevada. A standard E.C.F.M.G. certificate is required for entrance to Board examinations by all states except 11. Thirty-nine states require one year of intern training in an approved hospital in the United States as a requisite for licensure. Eleven boards examined more than 75 foreign graduates. New York, Illinois, Pennsylvania, New Jersey, and Virginia were the first five states of these eleven.

Foreign graduates come from the following areas: Far East, 38%; Latin America, 19%; Near and Middle East, 17%; Europe, 15%; Africa, 2%; Others, 11%.

During the period from 1946 to 1963, 20,841 foreign graduates were licensed in the United States. At the present time, 23% of the interns and residents in United States hospitals are foreign graduates. There are 942 foreign medical students enrolled in United States medical schools.

North Dakota: At the present time, there are 49

foreign graduates licensed and practicing in North Dakota: 28 in the specialties and 21 in general practice.

During 1964, 9 foreign graduates were examined by the North Dakota State Board of Medical Examiners, 5 of whom passed and 4 failed. There were no failures among the United States and Canadian graduates (the latter are not considered foreign graduates).

The original idea of the imports of F.G. (Fulbright Exchange Students) was to invite foreign M.D.'s here and place them in approved hospitals for three years training. Then they were to return to their native lands and help elevate the standard of medical care there. The facts appear to be that the majority did not return, but remained in this country as evidenced by the fact there are now over 20,000 licensed in the United States and an undetermined number, at least in the thousands, who are here, but not licensed.

Respectfully submitted,
(Signed) C. J. GLASPEL, M.D., *Chairman*
Committee on Foreign Trained Physicians

Committee on Diabetes

Members of Committee: Drs. E. A. Haunz, Chairman, Grand Forks; D. M. Barnard, Fargo; B. Hordinsky, Drake; Warren R. Jensen, Valley City; E. O. Hieb, Jamestown; W. H. Wall, Wahpeton; D. G. McIntyre, Rugby; G. H. Heidorn, Minot; K. G. Foster, Dickinson; and P. F. Klosterman, Bismarck.

The Committee on Diabetes, initiated by Dr. Leonard Larson of Bismarck, has continued its primary function to encourage and coordinate annual diabetes detection drives throughout the State under sponsorship of constituent local medical societies. This function is a cooperative effort in support of National Diabetes Week, sponsored in November each year by the Committee on Detection and Education of the American Diabetes Association, Inc. Increasing participation is in evidence among district medical societies throughout the nation. Last year, well over one thousand societies held individual detection drives.

Unfortunately, during 1964 there was virtually no activity in diabetes detection throughout the State of North Dakota with the exception of a very limited drive among Boeing employees engaged in missile installation at the Grand Forks Complex. Approximately 600 tests were performed, and the final results were not available at the time of this writing. However, this limited drive points up the fact that there is continuing interest on the part of the public in diabetes detection.

Our committee has also been approached by the State Health Department for participation in diabetes detection. In 1965 it is hoped there may be some cooperative effort made jointly between the local medical society and the North Dakota State Public Health Department to carry out diabetes detection programs. The committee feels that it is most important that the medical profession throughout the state try to maintain the initiative and leadership in this overall project. In fact, diabetes detection drives throughout the United States have been almost exclusively carried out under the sponsorship of local medical societies. This not only stimulates more enthusiasm among participating physicians but sustains the good will which has been engendered toward the medical profession in carrying out this free service to the public throughout the past decade.

This committee sincerely hopes that constituent medical societies of the North Dakota State Medical Association will give serious thought to carrying out some sort of diabetes detection program in 1965. The expense involved in these drives is minimal because of the cooperative effort of various pharamceutical manufacturers in furnishing free testing material and the American Diabetes Association, Inc., is glad to cooperate in furnishing publicity materials to assure a uniformly ethical approach throughout the different projects.

I would again like to express my appreciation for the continued excellent cooperation from committee members throughout the year who stand ready to cooperate at any time detection programs are initiated by individual groups.

Respectfully submitted,
(Signed) E. A. HAUNZ, M.D., *Chairman*
Committee on Diabetes

Committee on Crippled Children

The Committee on Crippled Children held a business meeting on December 12, 1964 at the Gardner Hotel in Fargo. Dr. Paul Johnson, Chairman, presided, beginning at 9:30 A.M.

Present were Drs. A. E. Culmer, Jr., D. T. Lindsay, D. W. Nagle, L. B. Silverman, J. D. Craven, B. A. Mazur, Ralph Vinje, G. M. Hart, Jon Eylands, James Little, G. W. Toomey and R. D. McBane. Also present was Daniel Buchanan.

A proposed Bill concerned with the Battered Child was discussed by the Committee. It was pointed out that through the enactment of such legislation in the State, there would be a means for the investigation of suspected cases of child abuse. Dr. Lindsay moved that the Committee support the proposed legislation. It was seconded by Dr. Nagle and carried.

There was a review by the Chairman and others of the State's CCS program. Dr. Johnson noted that over the past five years, the diagnoses of greatest frequency have been strabismus, cleft lip and/or palate, congenital malformations of the circulatory system, and cerebral palsy. This, he said, was quite a contrast from primarily orthopedic diagnoses in the first years of CCS. In spite of the change in diagnoses, however, Dr. Johnson pointed out that the number of cases approved for CCS had remained quite stable at around 480 a year.

It was brought to the attention of the Committee that the attending physician in CCS cases has the option to indicate whether or not he wishes follow-up care for the patient. Such a determination is to be made on the CCS reporting form.

It was also noted that one member of the Advisory Committee to CCS was appointed by the State Medical Association, and that the Association had a direct link to CCS through that physician.

Mr. Orville W. Hawes, Executive Director of the Easter Seal Society, spoke about the pilot program of remedial reading the Society had conducted the previous summer at Camp Grassiek. Mr. Hawes said he felt the children had shown improvement from the program, and that it was planned to repeat the project in 1965. After some discussion, the committee voted to lend its endorsement to the 1965 remedial reading program of the Society.

Members of the committee next discussed the role of the Public Health Nurse or welfare caseworker in follow-up care. They agreed the physician should make the determination of what type of home care or follow-up, if any, is desired. They also reaffirmed a statement in this regard, taken from the annual report to the House of Delegates of the Association's representative to CCS. The Statement: "It should be the option of the parent or the physician whether nursing or social services are needed or

wanted and should not be given on the basis that when individuals are on a public program, such are automatically needed."

There being no further business, the meeting was adjourned.

Respectfully submitted,
(Signed) PAUL L. JOHNSON, M.D., *Chairman*
Committee on Crippled Children

Committee on Aging and Rehabilitation

The Committee on Aging and Rehabilitation met once during the year, on December 12, 1964, in Fargo. The results of this meeting were the following recommendations:

1. Continued agitation for the utilization of the Rehabilitation Unit of the Medical Center of the University of North Dakota.
   A. Touring exhibit of the Rehabilitation Unit to be displayed at hospitals, clinics, etc., throughout the State.
   B. At the 1965 Annual Meeting of the North Dakota State Medical Association:
      1. Exhibit or display of the facilities available at the Rehabilitation Unit.
      2. Informal or formal tours and teaching demonstrations at the Rehabilitation Unit itself.
   C. Reminding the members of the House of Delegates to remind the members of their District Medical Societies to remember to utilize the Rehabilitation Unit.
2. Urging the nursing homes in North Dakota to apply for accreditation by the National Council for Accreditation of Nursing Homes.
3. Support of the broadening and liberalization of North Dakota's M.A.A. law.

Respectfully submitted,
(Signed) HAROLD W. EVANS, M.D., *Chairman*

Liaison Officer to the North Dakota State Bar Association

This Representative attended the American Medical Association, American Bar Association Medicolegal Conference at Las Vegas, Nevada, held from March 11 through March 13, 1965. This excellent conference was directed toward helping the physician in both personal and professional legal matters and was felt to be a very excellent conference. Approximately 1,750 members of the American Medical Association and American Bar Association were present with the number nearly equally divided between the two Associations.

A local Medicolegal meeting was held in Bismarck in November, 1964, bringing together members of the Sixth District Medical Society and the Fourth Judicial District Bar Association and some additional members of the territory immediately surrounding the Fourth Judicial District. A panel of three members of the Sixth District Medical Society and three of the Bar Association discussed the medical and legal aspects of three different topics and it was felt that this presentation was quite informative and enthusiastically received. It is recommended that this plan be attempted in the other District Medical Societies.

Consideration of a State-wide Medicolegal conference was considered, but because of many factors including the legislative year, it seemed that it was impractical for this time. Further consideration should be given to this in the future since it is felt that this, too, might aid in continuing to develop the excellent rapport existing between our several groups.

Respectfully submitted,
(Signed) PAUL L. JOHNSON, M.D., *Representative*

Liaison Committee to the North Dakota State Dental Association

There has been no activity during the past year to report except for aid to the Dental Association in regard to the possibility of a school for dental hygienics to be located at the State School of Science, Wahpeton, North Dakota. Further support by the Medical Society in this direction should be considered during the ensuing year.

Respectfully submitted,
(Signed) DAVID G. JAEHNING, M.D., *Representative*

Committee on Pharmacy

In spite of the fact that many questions involving pharmacist-doctor relationship should be resolved, for some reason or other the Committee on Pharmacy never met last year.

Questions such as (1) How far can a pharmacist go recommending so-called "home remedies?" (2) Should drugs be prescribed by generic or trade names? (3) Is it permissible or ethical to substitute a trade name product for a similar product with a different trade name? (4) How can the sale of non-prescription narcotics, barbiturates, amphetamines, etc., be controlled? (5) What should the relationship be between a "doctor controlled pharmacy" and the medical profession? Together with similar questions need these answers. Who should initiate the call for round-table discussions?

Respectfully submitted,
(Signed) O. A. SEDLAK, M.D., *Chairman*
Committee on Pharmacy

Report of Representative to Medical Center Advisory Council for the Year 1964-65

STUDENTS

The fall of 1964 freshman class was made up of 44 students, 31 of whom were North Dakotans. The admission policy is to fill the class as nearly as possible with qualified North Dakota students giving second priority to applicants from Western Minnesota and Montana.

No matter how careful the selection, we lose from three to six students from each class for various reasons in the freshman year. These places are usually filled with graduate students in the sophomore year. Last year we transferred 47 students, the largest number in the history of the school.

In the fall of 1965, it appears that we may fill the whole class with North Dakota applicants. We already have 60 applications from North Dakota students and if 44 of these turn out to be qualified, this will be the first time in many years that a full freshman class has been filled from the State.

In March, 1965, there are 40 students in the Graduate School: twenty-two (22) in Biochemistry, eight (8) in Anatomy, four (4) in Microbiology, and six (6) in Physiology-Pharmacology.

In 1964, six Ph.D. degrees were given in Anatomy, four Master degrees in Physiology-Pharmacology, and three Master and three Ph.D. degrees in Biochemistry.

RESIDENCY TRAINING PROGRAM

The Pathology Department Residency Training Program continues to progress with four residents in train-

ing most of the time. These students receive all of their training at the University of North Dakota Pathology Department. The program is fully accredited.

At present, arrangements are being made with Quain and Ramstad Clinic in Bismarck for necessary Basic Science Instruction for residency training programs in Radiology, Internal Medicine, and Surgery. This will be at no cost to the Medical Center.

FACULTY

Since the last report, the school has added Dr. Frank Low as a Hill Research professor in Anatomy. Dr. Low is an experienced electron microscopist.

Dr. Gerard Obert resigned to accept a position in the Pathology Department at the Neuropsychiatric Institute in Fargo.

Dr. Peter Isaacson, a former resident in Pathology, now taking advanced work at Harvard, will join the faculty as an Instructor in Pathology on July 1, 1965.

A head of the Department of Physiology and Pharmacology to replace Dr. Potter has not yet been obtained.

Dr. Szyrynski resigned in November, 1964. He has been replaced with Dr. Blaine McLaughlin, a qualified and experienced psychiatrist who has been on the staff of the Women's Medical College in Philadelphia for 19 years. Dr. McLaughlin is interested in community psychiatry programs, will be active in the teaching program at the Medical School, and will conduct limited private practice in Psychiatry.

Dr. Donald Barcome, a qualified physiatrist, has accepted an appointment as director of the Rehabilitation Center starting in July, 1965, and will also teach Physical Diagnosis.

Faculty compensation continues to present some problems, particularly at the professor and associate professor levels. Attention is being given to this problem.

PSYCHIATRIC TRAINING PROGRAM

To date a total of $70,800 of Medical Center Mill Levy funds has been committed for psychiatric training of physicians and one social worker or psychologist. Of five physicians receiving training under this program, three are now practicing in the State and two are due to return here, one in August, 1965, and the other in July, 1966. Starting in 1964-65, one social worker is receiving training for psychiatric work under this program.

STUDENT LOAN FUNDS

It appears that between the Mill Levy Loan Fund, the American Medical Association Loan Fund, and the Federal Government Loan Fund, adequate money is available to those who need financial help to complete medical school. We now have about $475,000 in Mill Levy funds tied up in Medical and Dental student loans. Some of these are being repaid and others are being forgiven for practice in smaller communities in the state. The net effect of this program on physicians returning to the State is still impossible to judge.

As of January, 1965, $21,000 was still available in Federal Loan Funds. Subsequently, this money has been loaned to 21 medical students. This program charges no interest until education is completed and then the interest is 4½% with ten years to pay. It is planned to be a revolving fund. This program may have considerable attraction because of the lower interest rate and ease of obtaining the loans. There are no forgiveness features, however.

Between the Federal and the AMA Loan Funds it is quite possible that the Mill Levy Loan Program may become less important, thus releasing money that we now have to earmark for the loan program and have tied up for an indeterminate period.

A recent study by Dean Harwood suggests that an increasing number of UND graduates may be returning to the State to practice. This is difficult to judge but the figures indicate that of the total number of physicians in the State and active as of 1965, 37.6% were UND graduates; in 1964, 33%; and in 1958, 28%. The study further indicates that 71% of North Dakota physicians listed as general practitioners in the State Board of Medical Examiners Directory are UND graduates.

BLOOD BANK

The Medical Center Blood Bank has been terminated. The transition was made very easily.

REHABILITATION CENTER

The load here continues to increase slowly. Admissions have increased from 104 in 1958-59 to 207 in 1963-64. The load varies considerably so figures as of this date do not have any great significance. Actually, as of this writing in March, 1965, we have eighteen inpatients.

Dr. Donald Barcome, a qualified physiatrist, now completing a year of teaching and research at the Baylor Medical School Rehabilitation Center in Texas, is scheduled to arrive in July, 1965, as Medical Director. He will also have a faculty appointment and teach Physical Diagnosis. At Baylor, Dr. Barcome has worked closely with referring physicians and is said to be familiar with the problems of patient referral to Rehabilitation Centers.

As reported in previous years, the work done at the Rehabilitation Center is high-quality work and the personnel could do a considerably greater volume. While the work has been in large measure supervised by the Orthopedic Surgeons of Grand Forks with other medical specialists available for consultation, this supervision has been part-time.

It might be stated that the chief criticisms of this program have been lack of volume of patients and the lack of a fulltime physiatrist. With the arrival of Dr. Barcome it would appear that at least one of the causes of criticism will be eliminated.

FINANCES

The cost of operation of the Medical School and Medical Center has gradually increased. From time to time new programs have been added, each of which has cost money. The nursing school now costs about $120,000 a year, the Rehabilitation Center costs $60,000 above income and Psychiatric training grants $14,800. We are required by law to earmark $75,000 for Medical Student Loan Funds and $25,000 for Dental Student Loan Funds. In addition, there is the Medical Technician School and a surprising amount of teaching of non-medical students such as those in Physical Education, St. Josephs School of Nursing and others.

Numerous Federal and private grants, some of which include supplementary funds for overhead, have enabled the Center to live within its income. We have now reached a point where the cost of operation of all these programs exceeds the Mill Levy income. In 1964-65, the Mill Levy income was $695,000 and the cost of operating the Medical School alone was $575,000. It is obvious that with the other demands on Medical Center funds, the total operation is running behind income. While we still have some reserves on which to operate, it is obvious that either some programs will have to be transferred elsewhere or we will soon have to approach the Legislature for supplementary funds.

We are advised that a large amount of Mill Levy

funds have been coming from personal property taxes. We assume that an equivalent amount of funds will in some way be directed to the Medical Center, but at this writing no one seems to be certain just how this will be accomplished.

Respectfully submitted,
(Signed) PHILLP H. WOUTAT, M.D., *Representative*
to the Medical Center Advisory Council

Governor's Health Planning Committee

I was appointed a member of this Committee on November 23, 1964. The Committee met on November 24, 1964. Nine projects were considered for Hill-Burton Fund aid. Out of these nine that were considered, the Committee approved the grant of aid to St. Josephs Hospital Addition at Minot and to the Missouri Slope Nursing Home at Bismarck. $75,000 and $9,000 were approved, respectively. This money is all that was available and it is believed that in the future more aid will be given as money becomes available.

Respectfully submitted,
(Signed) M. A. K. LOMMEN, M.D., *Member*
Governor's Health Planning Committee

Committee on Liability Insurance

The Committee on Liability Insurance did not meet during the year and no problems were brought to the attention of the Committee.

Respectfully submitted,
(Signed) JOSEPH SORKNESS, M.D., *Chairman*
Committee on Liability Insurance

Committee on Cardiovascular Diseases

The Committee on Cardiovascular Diseases held no formal meetings and were not asked to consider any problems in the past year. It is anticipated that this Committee may be concerned with the President's recent proposals to conquer heart disease, cancer, and stroke. This program could have far-reaching effects as far as the practice of medicine is concerned in our State.

Respectfully submitted,
(Signed) R. D. STORY, M.D., *Chairman*
Committee on Cardiovascular Diseases

Committee on Emergency Medical Service

The Emergency Medical Committee failed to meet in the past year due to scheduling and poor attendance. However, in the past year, the Public Health Department has been active in this work through Mr. Robert Freise and Mr. Larry Anderson meeting with the Committee of the District Societies.

Several exercises were held: one at Dickinson in November, 1964, Devils Lake in October, 1964, Williston in September, 1964, Hebron in 1964, and Grand Forks in March, 1965, in conjunction with MEND of the Medical School. These exercises created interest generally but had only fair physician participation.

It is strongly urged by this Committee that all Hospital staffs prepare an Emergency Medical Plan and run one or more exercises each year.

Respectfully submitted,
(Signed) RALPH E. MAHOWALD, M.D., *Chairman*

Report of the Representative to the Crippled Children's Services Division Public Welfare Board of North Dakota

A meeting was held October 17, 1964, at the State Capitol, Bismarck, North Dakota. The following members were present: Drs. James R. Amos, Ralph J. Dunnigan, W. G. Garrett, V. G. Borland, and Donald E. Skjei. Dr. J. J. McLeod and Dr. F. D. Naegeli were absent. Public Welfare staff present were: Dr. P. W. Freise, Leslie O. Ovre, T. N. Tangedahl, Margaret Lister, Helen Wahlund, and Phyliss G. Wigen.

First, there was a discussion by the members of the Medical Advisory Committee on the difficulty of the Medical Director's assigning a working diagnosis on some clients because of limited information available in the social service report or medical report, if present; and also whether Crippled Children's Services diagnostic evaluation should include basic laboratory work, such as hemoglobin, urinalysis, and leukocyte count; or whether diagnostic evaluation should continue to be limited to specific laboratory tests and X-ray in connection with the evaluation of the specific problem. There followed some discussion by the different members of the Medical Advisory Council. It was finally decided that other than specific laboratory work and X-ray, other laboratory work should not be included in the Crippled Children's Service Program.

The next topic of discussion was in respect to kidney transplants. The final opinion of the Board after discussion was that this particular procedure is still of an experimental nature and that it should not be included in the Crippled Children's Services.

The next area of discussion was that of hearing loss which was added to the Crippled Children's Service Program in June, 1963. At the present time, the Program does not include a provision for hearing aids or hearing therapy, although Crippled Children's Services does pay for hearing aid evaluation to determine if an aid is indicated, and, if so, the type recommended. It was the consensus of the group that (1) there should be further study of the needs in this area, (2) it be determined how many would need hearing aids, (3) if we can get used hearing aids, Crippled Children's Services make an effort to do so, and (4) Crippled Children's Services stay out of the area of purchasing hearing aids this year.

The next item on the agenda was services for the mentally retarded. It was stated that the North Dakota Crippled Children's Service Program has approximately $15,000 specifically earmarked for services for the mentally retarded for the fiscal year. The Crippled Children's Service plan, as presently approved by the Children's Bureau, provides for the use of these funds in the following 4 areas: (1) dental care, including hospitalization, to perform the dental care for the mentally retarded individuals, (2) expansion of diagnostic services, (3) genetic testing, and (4) employment of a physical therapist who would be assigned to provide therapy to the mentally retarded children at the Grafton State School. After considerable discussion, the consensus of opinion was that the group was least interested in having the funds used to employ a physical therapist to be assigned to the Grafton State School, and indicated considerable enthusiasm for expending funds for genetic testing. The group concurred in the need to provide dental services for the mentally retarded who require hospitalization for such.

The next topic for discussion was payment for therapy by massage therapists. It was the unanimous decision of the group that Crippled Children's funds are not to be expended for purchase of therapy provided by massage therapists.

The next discussion by Mr. Tangedahl was the proposed legislation regarding abused and abandoned children. The purpose of this was to inform the group of the situation and of proposed legislation.

The next topic was provision of drugs for children with brain damage and convulsive disorders. There was some discussion of the use of medications for children who have brain damage and convulsive disorders. It was decided after discussion that this program would not include provision of drugs for children with brain damage and convulsive disorders.

The release of medical information was next considered by the group. Mr. Tangedahl stated that at a meeting of the medical council a year ago, there had been considerable discussion of follow-up by Crippled Children's Service, and it was decided that the purpose of such should be twofold: (1) to preserve the doctor-patient relationship by making the situation of Crippled Children's Services as much like that of the private patients as possible, and (2) to provide a positive approach to follow-up by Crippled Children's Service in order that such may be effective, as unwanted follow-up has little, if any, value to either the patient or the physician. The question was raised whether there should be a specific permit for release of medical information if the parent requests public health nursing follow-up, and if the physician has not indicated such when submitting his report to Crippled Children's Services on report form PW 52. It was decided that a general letter be directed to the doctors suggesting that they ask their secretaries to remind them of the need to consider such follow-up care when submitting their reports to Crippled Children's Services.

The last item of discussion was that of cases where prolonged medical and hospital care is necessary for a child with considerable brain damage following surgery for a congenital cardiac problem. No definite conclusions were reached except that there was going to be some exploration of the possibility of transferring this child to San Haven from a hospital in Minot.

Respectfully submitted,
(Signed) Donald E. Skjei, M.D., *Representative*

Committee on Constitution and By-Laws

There was no formal meeting of the Committee on Constitution and By-Laws for the business year 1964-65.

Our Committee contemplates a change in Section 1, Chapter II of our By-Laws, which now states: "The annual session shall be held for four consecutive days beginning on a Saturday, which period of time shall include the first Sunday in May." This change has already been recommended by our House of Delegates on December 13, 1964, at Fargo. The recommendation was that the sessions not be four consecutive days as noted above, but on Friday, Saturday and Sunday at approximately the same calendar time. Final action on this recommendation will most probably be acted upon by the House of Delegates in our May meeting in 1965.

We are also giving special consideration to changes in our Committee system. We recommend five or six Commission Chairmen with groups of our existing Committees under each. Councillors may well be considered as Chairmen of these Commissions. This change would then bring better coordination and communications between the House of Delegates, Councillors, Committees and State Officers.

We are attempting to get further information from other states who have gone to the Commission System, and still feel that further information is necessary before we recommend this change.

I recommend that this Committee be continued for the following year.

Respectfully submitted,
(Signed) A. R. Gilsdorf, M.D., *Chairman*
Committee on Constitution and By-Laws

Committee on Medicine and Religion

The Committee on Medicine and Religion has attempted during the past year to orient the State Committee on some of the purposes and methods in promoting our program among the physicians and clergymen of this State. Most of the members of the Committee and some of the local district committees, have been contacted personally by the Chairman.

Attempts to have meetings of the Committee have been frustrated by a difficult winter for traveling and many conflicts. A meeting scheduled in October at Jamestown, during which we had planned to use the State Hospital Chaplains in presenting our program, had to be cancelled because of too many previous commitments and conflicts among committee members. We were able to have a meeting in January in Fargo, at which time Father Benson from the State Hospital, Pastor Johnson, a hospital Chaplain in Fargo, Dr. Melton, Chairman of the First District Medicine and Religion Committee, and Mr. Etheridge, from the AMA office of Medicine and Religion were present. These men gave us insights into ways in which the clergymen can be of assistance to the physician in the better care of his patients, and also ways in which the physician can contribute positively to the work of the clergymen. A film strip was shown at this meeting, also, which dealt with several of the aspects of the local committees on medicine and religion. This film strip is available through the State Office for any of the local committees to use.

The local medical societies have been encouraged to appoint their committees on medicine and religion and most of them have done so. It is hoped that the local medical society Presidents will take an active interest in this program and encourage their local committees to present at least one program a year to the local medical society.

State-wide publicity is being planned, and we plan to show the movie, "The One Who Heals," at the State Medical Association Convention this year. We have requested an exhibit from the AMA for the State Meeting, but were unable to get it for the dates that we wanted it.

Your Chairman attended a workshop on Medicine and Religion in San Francisco on the Friday and Saturday preceding the American Medical Association Meeting in June of 1964. The results of this workshop have been published and will be found very useful in the local society's program. Each district chairman will be sent a copy of this report.

Respectfully submitted,
(Signed) M. J. E. Johnson, M.D., *Chairman*
Committee on Medicine and Religion

Committee on Mental Health

This past year has proved to be a year of additional milestones being established for the betterment of the Mental Health Programs within the state of North Dakota. There is an ever increasing lay interest in this because of the stimulating activities of the North Dakota Mental Health Association which includes many physician members. The program of the State Health Department on Mental Health and Mental Retardation evaluation in various sections of the state has been actively engaged in by physicians who have helped to contribute to the statistics and participated in the planning conferences for Mental Health and Mental Retardation services throughout our state.

Two meetings of our committee have been held during the last year; the first, a joint meeting with the Board of Directors of the North Dakota Mental Health Association, as well as with members of the Legislative Committee of

the State Medical Association. At that meeting a great deal of interest was expressed in the Community Mental Health Center Bill and recommendations made regarding some of the wording in the bill no doubt were of value in the eventual passage of the bill. One of the primary things accomplished, however, was a chance for a lay group and groups from the Medical Association to work together for their common interests. This bill will no doubt be carried into action relatively soon in some of our communities, at least within the areas of Grand Forks and Fargo, having active groups working for the establishment of such Community Mental Health Services. It is noted too that a Mental Health symposium was to be held in April at the University of North Dakota Medical School to concentrate on the attention that needs to be placed upon the development of Mental Health facilities in our state. For this meeting the president of the American Psychiatric Association, Dr. Daniel Blain, was to be the principal participant.

In December at the Interim Session of the Council and House of Delegates an outstanding turn-out of members was obtained. There were eleven (11) members of our association as well as three other physicians attending the meeting. A review was made of the items of Mental Health interest that were to come before the forthcoming 1965 state legislature. It was recommended by the committe that the Community Mental Health Services Bill be approved in principle. Other bills that were considered were the request for the building of an Adolescent Treatment Center at the State Hospital. This bill was also supported. Consideration of the bill to transfer the State Institutions to the State Health Department was made and this bill was supported in principle. On presentation of all these recommendations to the House of Delegates, they were all approved in principle, and our association backed these bills during the legislative session. As previously mentioned, the Community Mental Health Services Bill did pass so that communities who desired to establish a Mental Health and Mental Retardation Service unit may do this and receive assistance from the state. It is, however, primarily a local responsibility to establish these units. The bill for funds for the building of an adolescent unit at the State Hospital did not pass the legislative session. The bill for the transfer of the State Institutions to the State Health Department succeeded only insofar as the State Hospital at Jamestown was transferred, with San Haven and Grafton failing to be included. Other bills that were of interest in the Mental Health field that passed were the so-called Battered Child Bill and the bill that broadens physician-patient privileged communication.

It is apparent that with the introduction of the new Community Mental Health and Retardation Services Bill that physicians are going to be called on in increasing numbers to take the responsibility and leadership within their communities for guiding the establishment of any Community Mental Health Center. This is a responsibility of the physician, not only to his own community, but to the medical profession in general. He should see that the proper guidance is obtained with medical orientation, so that the establishment of any psychiatric services within the community are: first, realistic, and second, under medical supervision, in order to provide patients and citizens the best possible type of care in the most economical way.

These are items that have been stressed in the past by not only your current chairman but by previous members and chairmen of our organization.

Respectfully submitted,
(Signed) A. C. KOHLMEYER, M.D., *Chairman*

REPORT OF THE DELEGATE TO THE AMERICAN MEDICAL ASSOCIATION

The 1964 annual session of the AMA House of Delegates was held in San Francisco. Key health issues, then under debate in Washington, were of major concern, and the timely action of the House Ways and Means Committee in rejecting King-Anderson legislation was enthusiastically received. The probable impact of the upcoming party conventions and November elections was subtly received by Delegates and others. The House approved a resolution that labeled cigarette smoking a health hazard, and advised all M.D.s to make this fact known "by every available means of communication." A strong statement on medical civil rights was adopted. Realizing that the involvement of physicians in continuing medical education is one of the greatest challenges in medicine today, a survey of voluntary accreditation programs in continuing medical education will be instituted by the Council on Medical Education, with a report forthcoming. An intensive report on Physician-Hospital relations was reaffirmed along the AMA's 1951 guidelines. The House reiterated its policy favoring federal grants for "bricks and mortar," construction and renovation of medical schools, hospitals, and related institutions, as well as mental health centers. It approved a study of the appropriate content of courses in "medical civics and economics" for medical students. Dr. Norman Welch was inaugurated President at this meeting, only to suffer an untimely death three months later. He was succeeded by Dr. Donovan Ward of Iowa.

The Interim Meeting was held the first week of December, 1964 in Miami Beach. The effects of the November elections on medical legislation were considered. The House of Delegates reiterated its stand against any form of a compulsory hospitalization program for the aging under Social Security, calling for the states and counties to implement fully Kerr-Mills and other existing programs "to the end that everyone in need, regardless of age, is assured that necessary health care will be available." The House, recognizing the socio-economic aspects of the population explosion, went on record by stating "the prescription of child-spacing measures should be made available to all patients who require them, consistent with their creed and mores, whether they obtain their medical service through private physicians or tax or community supported health services." The House accepted 33 recommendations from the Commission on the cost of medical care. These recommendations, among others, noted that physicians exercise an important influence on the cost of medical care, and should be cognizant of the cost of all services and supplies prescribed for patients. This report, which is extremely well done and illuminating, is available from the State Office or AMA headquarters. The House also endorsed the formation of hospital utilization committees, "inasmuch as the judicious use of hospital facilities by the public and physicians is essential to the efficient and economic functioning of the prepayment and voluntary health insurance systems." We approved the establishment of a teletype network between AMA headquarters and the State Medical Societies for improved and more rapid communications. The House urged the Medical Societies to approve, where feasible, the inclusion of a voluntary non-deductible contribution to independent political action committees on the Society's annual dues billing statement. The House paid tribute to the late Drs. Norman Welch and Paul Carlson. James Appel, M.D., was elected President-Elect.

A special session of the House of Delegates was called

in Chicago on February 6 and 7, 1965, and voted to "enthusiastically support" the Association's Eldercare program, as embodied in the Herlong-Curtis Bill and similar legislation, now pending before Congress. It also called on the Board of Trustees and two AMA Councils to investigate the possibility of expanding the Kerr-Mills programming to provide aid for the medically needy of all ages. The funds for implementing an educational effort in support of Eldercare were authorized from the AMA treasury.

It remains my deep conviction, after being privileged to observe the policy-making body of the AMA in action for several years, that this, indeed, is a dedicated body of physicians who faithfully attempt to interpret their constituencies' philosophy in formulating the programming of the American Medical Association. The prime concern of the AMA remains better health care for all people, and the overwhelming majority who speak for their constituent and component societies seem convinced that such is outside the province of federal control.

I personally feel that improved communication with District Societies is necessary for proper formulation of AMA philosophy. The individual physician must be aware of actions past and present, including the history and premises of AMA in order to influence others. Your Delegate has been privileged to appear before three District Societies this past year, and it is my hope that the AMA Delegate might meet once a year with each District Society.

I again urge North Dakota physicians to acquaint themselves with the action of the House of Delegates as reported in J.A.M.A. in the second issue that follows the annual and interim conventions. The volume of material and subjects considered in depth seems to increase yearly. I would welcome any suggestions and help from the North Dakota physicians, individually or collectively.

Dr. Willard Wright of Williston, Chairman of the Council on Medical Service, will be nominated for the office of President-Elect of the AMA at the June meeting in New York. He will be one of three nominees for this office of whom we know. Your support in encouragement of his candidacy is solicited. I should like to thank Dr. Wright, Dr. Robert Painter, my alternate, Lyle, and Dan for the assistance that is needed and graciously given, at these meetings.

Respectfully submitted,
(Signed) THOMAS E. PEDERSON, M.D.
Delegate to the AMA

FOREWORD

In accordance with the intent of Resolution Seven adopted by the House of Delegates, in annual session in Minot, in May, 1964, the headquarters office of the Association has prepared this informational material about the House of Delegates for use by the members of that body.

The material here is taken from the Constitution and By-Laws of the North Dakota State Medical Association, as adopted by the House of Delegates in June, 1957. We have attempted to express the duties and prerogatives of the House of Delegates in nontechnical language, so far as was possible. However, the Articles of the Constitution and the Chapters of the By-Laws are noted in each case so Delegates may refer to the specific language involved.

AUTHORITY OF THE HOUSE

The House of Delegates shall be the governing body of the Association and shall consist of the Delegates of the component Societies that elect them. It shall conduct all business of the Association except such as is otherwise provided for by the Constitution and By-Laws.

All recommendations of the House of Delegates dealing with the acquisition or disposal, of property of any kind, or with the appropriation or expenditures of funds in any way, must be approved by the Council.

(Const., Art. 5)

APPORTIONMENT

Each District Medical Society may send one delegate or his alternate to the House for every fifteen (15) paid-up members, or major fraction thereof.

(By-Laws, Chap. 4, Sec. 2 and Chap. 9, Sec. 2)

However, each Society shall have at least one delegate, regardless of the number of its members.

(By-Laws, Chap. 4, Sec. 2)

SEATING AND VOTING

Regular Delegates are seated in the House and may vote.

(Const., Art. 5 and By-Laws, Chap. 4, Sec. 2)

Alternate Delegates may be seated, but may not vote when the regular Delegate is present.

(By-Laws, Chap. 4, Sec. 2)

In case neither the regular delegate, nor his alternate is present, the Speaker of the House may appoint a substitute from the appropriate Society. The substitute shall be seated, and may vote.

(By-Laws, Chap. 4, Sec. 2)

The Speaker of the House may not vote unless his is the deciding vote.

(By-Laws, Chap. 6, Sec. 5)

These persons may have the privileges of the floor of the House, but may not vote: President, President-Elect, 1st Vice-President, 2nd Vice-President, Councillors, Secretary, Treasurer, Past Presidents, AMA Delegate, AMA Alternate Delegate.

(Const., Art. No. 5)

All meetings of the House of Delegates are open to members of the Association.

(By-Laws, Chap. 4, Sec. 3)

PRESIDING OFFICER — SELECTION

The Speaker or Vice-Speaker shall preside at the meetings of the House of Delegates.

(By-Laws, Chap. 6, Sec. 5)

The Speaker is elected for a one-year term by the House of Delegates at its Annual Meeting.

(Const., Art. 9, Sec. 3)

The Vice-Speaker is elected for a two-year term by the House of Delegates at its Annual Meeting on alternate years.

(Const., Art. 9, Sec. 3)

Neither the Speaker nor the Vice-Speaker are required to be members of the House of Delegates.

(Const., Art. 9, Sec. 3)

OFFICERS ELECTED BY THE HOUSE

The President, President-Elect, First Vice-President, Second Vice-President, Secretary and Treasurer shall be be elected annually by the House for a one-year term.

(Const., Art. 9, Sec. 2)

Councillors are elected annually by the House for a three-year term. A Councillor is limited to two consecutive terms, except in instances where he is elected to fill an unexpired term. In the latter case, he may serve the

balance of the unexpired term, plus two consecutive terms.

(Const., Art. 9, Sec. 2)

Representatives to the House of Delegates of the American Medical Association, in accordance with that body's Constitution and By-Laws, are elected by the House.

(By-Laws, Chap. 4, Sec. 7)

The President shall announce the names of a three-member nominating committee during the first session of the House at Annual Meetings. This committee shall submit its report to the House during its second session. However, additional nominations are to be called for by the Speaker or Vice-Speaker before an officer has been elected.

(By-Laws, Chap. 5, Secs. 2 and 3)

All elections are to be by ballot, with a majority vote necessary for election. In the event there is only one candidate for an office, election may be by acclamation, with unanimous consent of the members of the House present and voting without ballot.

(By-Laws, Chap. 5, Sec. 1)

FUNDS AND EXPENSES

Funds are to be raised by an equal per capita assessment on the membership, with the amount set by the House.

(Const., Art. 10)

QUORUM

A majority of the registered delegates shall constitute a quorum for the transaction of business.

(Const., Art. 5 and By-Laws, Chap. 4, Sec. 3)

SPECIAL SESSIONS

Special Sessions of the House of Delegates may be called in the following ways:

1. By the President;
2. By the unanimous consent of the Council's Executive Committee;
3. By petition of ⅔ of the Delegates.

(By-Laws, Chap. 2, Sec. 2)

AMENDMENT OF CONSTITUTION

Constitutional amendments may be approved at Annual Meetings only, by a ⅔ vote of the House of Delegates.

Amendments of the Constitution may be proposed in this manner:

1. Introduced in the House at an Annual Meeting, to be acted upon at any subsequent Annual Meeting;
2. Submitted by the Chairman of the Council, and;
   A. Published in the Journal-Lancet at least 3 months before the Annual Meeting which will act upon it, and;
   B. Sent by the Chairman of the Council to each District Society at least 3 months before the Annual Meeting which will act upon it.

(Const., Art. 13)

AMENDMENT OF BY-LAWS

Amendments of the By-Laws may be approved at Annual Meetings only, by a ⅔ vote of the House of Delegates.

However, amendments of the By-Laws may be introduced at any session of the House, but shall be tabled until any subsequent Annual Meeting.

(By-Laws, Chap. 14)

REFERENDUM

A question pending before, or passed by the House of Delegates, may be referred to the membership of the Association in the following ways:

1. By a ⅔ vote of the members at any general (or Annual) meeting;
2. By a ⅔ vote of the House.

A majority of the members voting shall decide the question and be binding on the House of Delegates.

(Const., Art. 11)

GENERAL DUTIES OF THE HOUSE

. . . Give diligent attention to and foster the scientific work and spirit of the Association

. . . study and strive to make each Annual Session a stepping stone to further ones of higher interest

(By-Laws, Chap. 4, Sec. 4)

. . . consider and advise as to the material interest of the profession, and of the public in those important matters wherein the public is dependent upon the profession

. . . use its influence to secure and enforce all proper medical and public health legislation, and to diffuse popular information in relation thereto

(By-Laws, Chap. 4, Sec. 5)

. . . make careful inquiry into the condition of the profession in the state

. . . adopt such methods as may be deemed most efficient for building up and increasing the interest in local societies

. . . organize the profession in counties where societies do not exist

. . . endeavor to promote friendly relations between physicians of the same locality

(By-Laws, Chap. 4, Sec. 6)

. . . provide and issue charters to District Societies

(By-Laws, Chap. 4, Sec. 8)

. . . revoke the charter of any component District Society whose actions are in conflict with the letter or spirit of the Constitution and By-Laws of the Association

(By-Laws, Chap. 12, Sec. 2)

SPECIAL ADDRESS

Speaker Christoferson next introduced two guests to the House: Mr. Sherwood Williams, Field Representative of the American Medical Association and Dr. Blair Henningsgaard, a delegate to the American Medical Association from the state of Oregon and a board member of AMPAC.

Dr. Henningsgaard's remarks follow:

DR. HENNINGSGAARD: Thank you very much for this privilege. My purpose here is selfish. As a member of the AMPAC Board I wish to state that the better you make your State PAC, the better we will look as a National Board. I am also pleading for the State PAC Board members whose job is often tedious and thankless. I think there are some ways which you, as members of your Association, could relieve them of some of this tedium. As members of the House you constitute the leaders in medicine in the state of North Dakota. I make a strong plea that you would join the State COMPACT and show the rest of the doctors that you support our objectives.

Our State PACS have each year been forced because of regulations to resolicit contributions and memberships. This seriously impairs their ability to carry out their political action. We like to think of these dollars from memberships as "hard dollars." If your State PAC is forced to use these dollars for mailings and overhead ex-

penses, their total political effectiveness is diminished. Various states have faced up to the reality of the situation and in many states the State Association finds it possible to make contributions to the Committee on Legislation who then in turn can contribute to the State PAC. None of these dollars go directly into a campaign. We have received contributions from other people who applaud what we have been doing.

Another way to assist this is in the form of combined billing. This relieves the Board of collecting memberships and releases them for their political activities. I understand most of these billings are done through your district societies; others are done through the state billings. In Pennsylvania, one county used the combined billing; Allegheny County left it up to the PAC for individual billing. Philadelphia combined the billing with a note that it was a non-tax deductible contribution. Their membership was in excess of 75%. Chicago went this year to combined billing and their membership jumped from 15% to 92%.

We would strongly urge that you consider these matters and give your State PAC all the help you can. The way all these men are working now, it is a very successful State PAC. Mark Andrews makes no bones about the effectiveness of AMPAC in North Dakota. We earnestly solicit your support.

Speaker Christoferson thanked Dr. Henningsgaard for his talk, and added that this matter of business would be brought up later in the sessions.

SPEAKER CHRISTOFERSON: I was struck rather forcibly with the large number of Past Presidents who are attending this meeting today and are still very active in the State Association. It seems to me to be worthy of note at this Session to bring to the attention of the Delegates what a wonderful group of Past Presidents we have who continue to take an interest in the Association to appear here and lend us their wisdom to our efforts.

I would like to take this opportunity to present to you some of the Past Presidents who are here. Our oldest Past President here is Dr. C. J. Glaspel, who was President in 1940 and 1941. The next Past President is Dr. Willard Wright who was President in 1949-1950. I would like at this time to ask Willard, a potential candidate for President-Elect to the AMA, supported vigorously by the Council and Members of the Association, to come up here and say a few words.

DR. W. WRIGHT: Thank you very much, Lee. This is an unexpected recognition. It has been my privilege to serve this Association and the AMA for a long time, but no one has brought up before that I was a Past President. My friend, Cy, looks younger than I do. I wonder if he did not cheat somewhere along the way.

I certainly appreciate the expression of confidence that you and the Council have given me today, and also Dr. Tom Pederson, who will nominate me for the office of President-Elect of the AMA. I certainly appreciate the support and help that all of you have given me here.

I have been with the North Dakota State Medical Association for a long time. In the early days we thrashed over our problems with Relief, New Deal and Welfare and we have gone on from there. It has been my privilege to be associated with the Council of Medical Service of the AMA and the task force of the Health Care for the Aged. Frank Coleman was on this with us. You can be assured in leadership his position in AMPAC is of the highest caliber. Joe Miller, Executive Secretary, got his start in AMA as Secretary of a Committee of which I was Chairman.

The doctors are very concerned with the situation in which we find ourselves. We are being handed legislation with which we are not in agreement. This poses a problem with the AMA which is required to understand, study and provide leadership in this situation. I will not go into the details of this story, but at the moment there is a bill before the Senate, which bill is in four parts—hospitalization; nursing home benefits to all persons over age sixty-five; the second part provides medical benefits in the home for persons over age sixty-five and extensive amendments to the Kerr-Mills program. The only basis of assistance will be the need. This is a welcome change and this part of the bill we are in favor of.

The final part consists of a multitude of proposals such as, the doctors to be included under the Social Security Tax structure; increased benefits to Social Security recipients; adding a number of aids to programs for children—all of which have medical implications. The AMA has been allotted the sum of fifteen minutes to present our case. We spent last weekend going over the testimony that we will present. We are going on record as being opposed to the whole thing, but if they insist on passing this, there are things they should do to make a better bill. At the moment the services of pathologists, anesthesiologists, radiologists and physiatrists are included in the doctor's portion of the bill and excluded from the hospital portion of the bill.

In the hospital section of this bill it provides a mechanism that the doctors should be the policemen for the government—to check that there would not be overutilization of these benefits such as 20 days in the hospital and 14 days in the nursing home. This to be done by a committee composed of the staff of the hospital, or appointed by other sources. This imposes an intolerable burden on the doctors to be policemen to save funds for the government, or try to save hospital care for people who will need it. It is certainly an involuntary servitude that doctors are expected to serve on these boards without remuneration. In a large hospital the number of man hours the doctors would have to put in on these committees would be very great.

The AMA is subject to much criticism—that we did not do this and should do that. Perhaps we deserve a lot of criticism. However, the doctors themselves should look back on their own affairs and indulge in a little self-criticism. There are many ways which we could look into our own affairs and decide to do better in this Association in this area. I think we have to admit that as an organization and individuals, we have not been sympathetic with, nor understood the tremendous social upheaval that this country has been going through. We have based our philosophy that certain things are wrong, or right. We are right in this philosophy but in the political atmosphere at this time the basic rules are wrong. We should never agree with it, but we should show it a little more understanding than we have in the past. Like it or not, we are going to have to live under these conditions for quite a while and we must stick together. The only basic organization in which we can stick together and accomplish someting is the AMA. We must have a strong National organization which will give the best leadership that you people can provide. We must operate on that level in as strong a way as possible. If you do not like the way the AMA is doing things, you can take it up with your North Dakota delegates to the AMA—Dr. Pederson and Dr. Painter.

I would be glad to answer any questions you may have if you wish to contact me. Thank you very much at this time for the privilege of appearing before you.

SPEAKER: Thank you, Willard. The next Past Presi-

dent from 1960 to 1961 is Dr. Carroll M. Lund; Dr. Ed Boerth from 1961-1962, and Dr. Amos Gilsdorf, our immediate Past President.

This year we have been very pleased with the outstanding work by our President, Doctor Dodds. It is my privilege to introduce to you, Dr. Dodds.

PRESIDENTIAL ADDRESS: "THE FUTURE OF MEDICINE"

DR. DODDS: The report of my activities and recommendations as your President for the past year is contained in the Delegate's Handbook. I am certain all of you have read this. Therefore, in the interest of brevity, I shall not allude to that report at this time.

My remarks will be limited to the future of medicine based on observations and thoughts brought into focus during the past year.

We of the Medical Profession are forced to accept the fact that the majority of the American voters have decided that the Federal Government will assume a greater role in the providing and financing of health care. I am acutely aware of all arguments pro and con dealing with government in the health field, although for years we have accepted this in some form at a state level. The recent action by the electorate indicate this body's acceptance of its inability to provide for advancing years, and its willingness to take another step toward total government management of individual income.

We are witnessing a world in revolution that will not return to previous economic and social standards. If we of the Medical Profession, regardless of past achievements, are not to become some of the pawns of this revolution it is mandatory that we develop enlightened, forward changes. It is also our responsibility to leave a desirable heritage to our successors such as we inherited from our predecessors.

I know of no military encounter that was ever won by fighting a series of delaying actions, yet we have been past masters in such tactics. All this while we were consoling ourselves by reiterating what we had accomplished, and we failed to take offensive action to win new fields.

In a flurry of activity, born of desperation, Eldercare was introduced to the present Congress. I can only ask—if this program, as proposed, is acceptable now, then why was it not proposed to the 86th Congress in 1959, prior to the Forand Bill?

In a survey recently conducted by the Association of State Medical Society Presidents, it was found that in some of the heavily populated states the membership in the American Medical Association left something to be desired. One state alone had 5,000 physicians that were non-members. Membership was also found to be low amongst the Medical Teaching Profession. This makes only one conclusion possible, namely that the AMA must be made more attractive so that all physicians will want to belong and participate. We are a democratic organization that will command respect and will speak with much authority for American Medicine. However, I think the AMA can be made stronger by listening to those who sometimes take issue with the majority's view—we should be a multiparty organization.

On April 16, 1965, Senators Douglas, Hartke, Moss and Neuberger introduced an Amendment to HR6675 which would include the services of Pathologists, Radiologists, Anesthesiologists and Physiatrists under the King-Anderson Part of the Bill. While I do expect full and complete hearings on HR6675 before Senator Byrd's Finance Committee, it is very important to all physicians that this amendment dealing with specialty services be deleted. Our leadership is alert to this needed action.

Recently my mail brought the action of one physician's group in which they resolved not to participate in any Government Medical Program. In theory, this approach seems good. Practically, to get the majority of physicians to cooperate is impossible. I think it is a negativistic approach that would only further tarnish the image of medicine and invite more drastic legislation. The experiences of physicians in Belgium and Saskatchewan should make that fact apparent. This is not appeasement once defined as "The Act of Throwing One's Friend to the Crocodile in the Hopes that you will be the last one eaten." Instead we must act to obtain more positive control over any Federal program, and this is not accomplished by playing the part of an ostrich and burying our heads to the facts of today. (Dr. Dodds read Dr. Blasingame's letter).

In the future, because of this revolution in medical care we shall find more hospital centralization of our practice so be active in your hospital and its administration. More physicians will be participating in the field of applied medical research. The effect of more Federal funds to medical education in addition to the 51 percent now provided will have a definite impact in the not too distant future. We, in medicine, must do everything to maintain our heritage, the public respect and our self esteem. We will increase our stature but this all will require clear thinking, more work, cooperation and possibly a few tears at the local and national level.

This House could consider a resolution to the AMA requesting that long range, positive planning be developed for the ensuing years. The Medical Profession should be alerted to the health needs of today and develop a spirit of cooperative understanding between Congress and the Administration in the hope that this will be of public benefit in a workable and mutually acceptable form. Also, the AMA should make such changes as are necessary to include all physicians and segments of the profession in an actively participating membership.

Total agreement with what I have said is not anticipated. It has been deemed my responsibility to make these statements rather than voice empty platitudes. If constructive arguments and enlightened thoughts are the product of my remarks, then my purpose has been served —Let there now be some positive action.

To Dr. Craven, your incoming President, I extend my sincere wishes for a fruitful year. To have served as your President this past year has been a rewarding experience and I take this final opportunity to thank all members of our Society for their loyal service, help and cooperation and to each, my deep appreciation of your trust.

Dr. Christoferson thanked Dr. Dodds for his very fine address and assured him that the House would act upon the four recommendations contained in his report in the Handbook. The Speaker added that certainly the town of Williston had produced more than its share of men who have contributed greatly to the Association. He next introduced Dr. Joseph Craven, President-Elect, whose Inaugural Address follows:

INAUGURAL ADDRESS

DR. J. D. CRAVEN: Gentlemen, it is with a sense of deep humility that I assume this office, so ably administered the past year by Dr. Alfred Dodds; nor is humility the only emotion that I experience.

They tell a story of two cows that were grazing along one of our great turnpikes, when along with the heavy flow of traffic there appeared a large stainless steel dairy

tank truck. Emblazoned on the sides of this truck were the words, "Sunburst Dairies—Our milk is homogenized, pasteurized, standardized and vitamin enriched." Whereupon seeing this the one old cow looked at the other and said, "Makes you feel kind of inadequate, don't it?" Inadequate, indeed gentlemen.

I am grateful, and I assume the office with no misconceptions.

In the Toastmaster organization a new member begins his participation by what is known as the "icebreaker" speech at which time he reviews his past life. I have no intention of any such recital; however, I am indeed grateful for the privilege of having been allowed to practice my profession the past 28 years in my home town of Williston.

For the past 28 years has truly been the golden era of medicine, scientifically speaking. The Chemotherapeutic era of treating disease began in 1936 with the advent of sulfanilamide and this was the year of my internship at Ancker Hospital. 1936 was followed by newer chemotherapeutic agents and subsequently by the antibiotic era and all of the other noteworthy advances by our profession, so well known to all of you. True, the scientific advances in medicine stagger the imagination.

Somewhat less gratifying, however, has been the encroachment upon our professional independence caused by the socialistic legislation that threatens to engulf American medicine despite our best efforts to forestall it.

Many of you have read the works of the great clinician Sir William Osler and you may have read his valedictory address given before the graduating medical students at the University of Pennsylvania just 76 years ago tonight. The title of his address was, "Aequanimitas" in which he exhorted the young graduating medical students to wrap themselves in a cloak of equanimity, to gird themselves against the rigors, trials and vicissitudes of that early day practice of medicine. Much of what he said seems pertinent to those of us in medicine today. I quote,

"There is a struggle with defeat which some of you will have to bear and it will be well for you in that day to have cultivated a cheerful equanimity. Remember too that sometimes from our desolation, only does the better life begin. Even with disaster ahead and ruin imminent it is better to face them with a smile and with the head erect than to crouch at their approach, and if the fight is for principle and justice, even when failure seems certain, where many have failed before, cling to your ideal and like Childe Roland before the dark tower, set the Slughorn to your lips, blow the challenge and calmly await the conflict."

Appropriate words indeed from out of the past!

Passage of the infamous King-Anderson legislation at this point seems inevitable despite the gallant efforts of organized medicine to defeat it. The AMA is only as strong as its constituent societies. Its strength flows upward from them. It is, therefore, desirable that all physicians take an active part in the affairs of their county and state organization.

Medicine cannot remain free to fulfill its destiny without a strong organizational structure and its organizational strength depends upon maximum support and participation by the members of the profession.

If passage of the King-Anderson bill does indeed become a reality, I would remind you that we have lost an important battle, but this does not necessarily mean the loss of the war or even the end of it. We must continue our efforts to defeat one by one the inevitable extensions and amendments to the legislation and the inroads that broadening of the bill make into the private practice of medicine.

The main problem in this country is not Medicare. It is not socialized medicine. The problem is far, far greater than this. The King-Anderson Bill and all that goes with it is just one of the small cancerous sores of the whole problem. Yet, it is not the problem, it is a manifestation of the problem. The whole problem in this administration goes much deeper than another attempt to socialize medicine in the form of a specific piece of legislation. Behind all words and implication lies the very basic issue of whether or not the American people are willing to submit to the loss of more and more of their individual freedom under the guise of security. The arm of medicine is just one appendage that the cancer of socialism is invading.

What incentive is there for the young physician to join his district society and to work hard to advance the cause of medicine at the district and state levels? Yes, and even at the national levels, as evidenced by the magnificent efforts of our own Willard Wright, Leonard Larson and Tom Pederson. What incentive is there, indeed, other than to save their economic skins, not having attained that station in life when one can be referred to as a sage.

I do, however, have some personal thoughts on the subject. There is great satisfaction to be derived from the busy practice of medicine because of the humanitarian nature of our profession and tangible rewards will follow. Most of us learn too late that, more rewarding than the tangible things in life are certain intangibles. I refer to something greater than anything else one can attain on this earth. I refer to the friendship of one's fellowmen, those with common interest.

As a child I recall a framed verse that hung on the wall in our home, indeed it now hangs in my home. It is a simple quotation from Phillip Brooks and reads as follows: "There is yet no culture, no method of progress known to man that is so rich and complete as that which is ministered by a truly great friendship." For, Gentlemen, man is not an island unto himself, nor does man live by bread alone. The returns from good works are always greater than the effort put forth.

Over the years, in my work with my district and state medical associations, if it had been my lot to have remained a worker in the vineyard, never having held a society office, never having headed a committee, I would have felt amply rewarded for all of the time and effort expended through you gentlemen and a host of other physicians throughout the state whom I have come to know as friends.

In contemplating my remarks before this society the past few weeks, my desire was not to present any burning message, nor to outline any startling program for the coming year, but rather to tell you what I feel in my heart.

It is only fitting at this time and in conclusion that I pay tribute to our outgoing president. How can I better do this than by saying it is my fervent wish that in the coming year I may as successfully carry out the duties of this office and project as favorable an image of medicine to the public as has been so effectively done by Dr. Alfred Dodds.

Dr. Christoferson thanked Dr. Craven and assured him that the members would work with him and for him to the best of their ability throughout the coming year.

Secretary Buckingham was asked to read the names of the Nominating Committee. The members are as follows: Amos Gilsdorf, chairman; Thomas Pederson and

Dr. Henry Norum. The House was advised that the report of this committee would be presented on the following day.

SPEAKER: It is always a delight for me to have the opportunity to come to this next item of business, because it makes me feel that one can stand up to the gaff of this profession of ours and reach an age of wisdom and truth. Since this is the time to present those Fifty Year Awards I would like to read the details on their lives and ask Dr. Dodds to present these men with their Fifty Year Member pins and certificates.

Dr. Vincent S. Irvine of Lidgerwood, N.D. was born September 18, 1889 at Dominion City, Manitoba, Canada. He graduated from Manitoba Medical College of Winnipeg in 1915 and was licensed in North Dakota in July, 1915. He practiced in Bantry, Larkin and Park River, N.D. before moving to Lidgerwood, N.D. where he also served as City Health Officer.

Dr. Dodds, will you please present Dr. Irvine with the Award?"

DR. DODDS: I have known you, Dr. Irvine, for a goodly number of years and when I signed this Fifty Year Award Certificate, I was amazed that a young man like you could have been here for fifty years. It is with sincere appreciation that I give you your Fifty Year Award.

DR. IRVINE: Thank you.

SPEAKER CHRISTOFERSON: The next gentleman who is here for his Award is Dr. C. J. Glaspel, of the Grafton Clinic, Grafton, North Dakota. Dr. Glaspel was born March 7, 1893 in Grafton; graduated from Rush Medical College, Chicago, receiving his diploma in 1915. He was licensed in North Dakota in July, 1915. He was President of the North Dakota State Medical Association for the year 1940-1941; Secretary of the North Dakota State Board of Medical Examiners from 1948 through 1961, and President of the Federation of State Medical Boards in the United States in 1958.

DR. DODDS: It is a tremendous pleasure to present this Award to you, Dr. Glaspel, when I recall that when I came to North Dakota you were "Mr. Medicine." On behalf of the Medical Association, I want to sincerely thank you for all the years of work and help that you have given to medicine.

DR. C. J. GLASPEL: Thank you.

SPEAKER: The third member of our Association who has reached his fifty years is Dr. Bakke. He is unable to be here today. Dr. Hans Bakke of Lisbon, North Dakota was born September 27, 1885 at St. James, Minnesota. He graduated from Marquette University, Milwaukee, Wis. January, 1915, and was licensed in North Dakota in January, 1916. He practiced in Lisbon and served his city as City Health Officer, Examiner of the Ransom County Draft Board and on the Insanity Board.

Dr. Bakke's pin and certificate will be mailed to him. He sent us a letter thanking us very much for the invitation and stated that he would be unable to attend this meeting.

SPEAKER: We have some unfinished business from our 1964 Annual Meeting in Minot, N.D. This is a resolution which was introduced at that time to the effect that the selection of a Councillor be made from a list of candidates given by the individual district societies. Dr. Dahl made a motion that the resolution be submitted back to the ten individual societies for their action to be brought up again a year from now at this meeting. I would like to refer this to reference committee number two, who will then refer it to reference committee number six, for action and presentation at the next meeting of the House. I have here several letters referring to this resolution which I will ask to be referred to the Resolutions Committee. I have here another letter from Mr. Buchanan which will be referred to Reference Committee number two and then sent to Resolutions Committee for their action.

Is there any further old business for recommendation and action? There being none, we will get on to New Business.

SECRETARY BUCKINGHAM: I have here a letter from Dr. Reichert, dated April 20, 1965, addressed to Dr. Lee Christoferson. Dr. Reichert is the Chairman of the State Board of Medical Examiners.

"House resolution No. 7 was passed during the recent session of the North Dakota Legislature.

"A resolution directing two members of the Thirty-ninth Legislative Assembly, together with two members of the State Board of Medical Examiners and two members of the State Board of Osteopathic Examiners, to study the feasibility of a single licensing board for both professions.

"That an interim committee be established consisting of two members of the Thirty-ninth Legislative Assembly, appointed by the Speaker, of which one shall be selected by the committee as chairman, and two members of the State Board of Medical Examiners and two members of the Board of Osteopathic Examiners appointed by the presidents of each board.

"As chairman of the State Examining Board, I appointed Robert Nuessle, M.D., and Joseph Cleary, M.D., present members of the State Board, and both of Bismarck, North Dakota, to represent the Medical Examining Board on this committee.

"I notified Mr. Vernon Wagner, Chairman of this committee, of my appointments. In fact, Dr. Cleary notified me that the first committee meeting took place in Bismarck on the evening of April 13th.

"I believe this M.D.—D.O. licensing resolution should be considered by our House of Delegates when they meet on May 1st."

ss. H. L. REICHERT, M.D., *Chairman*,
N.D. State Board of Medical Examiners

SPEAKER CHRISTOFERSON: I would like to ask Dr. Cleary if he would present before the House, the outcome of their meeting and the contents of this business.

DR. CLEARY: Gentlemen: You all have a copy of this information in front of you, entitled M.D.-D.O. The very first part relates to House Bill 901, relating to the definition of Osteopathic Surgeons. This Bill did not come out of Committee. Item number three is the result—which is House Resolution No. 7. The Speaker of the House appointed a committee, and this committee met on April 13, 1965. The Committee members are Representative Vernon E. Wagner of Bismarck; Representative M. T. Obie of Grand Forks; Dr. Robert Nuessle of Bismarck, and myself, and M. J. Hydeman, D.O. of Bismarck and Georgianna Pfeiffer, D.O. of Fargo.

Under item 3, I have listed the definition of Osteopathy; following this I have statements from Dr. Newman who spoke to the Federation of Medical Boards in Chicago in February. Dr. Newman is Chairman of the AMA Commission on Osteopathy and Medicine, and he is very favorable to combining medicine, or medical doctors and doctors of osteopathy. He feels that osteopaths are now practicing scientific medicine, listing six reasons for his belief.

On page three, I have listed several facts and figures about osteopaths. In forty states they have unlimited practice and in twenty-four states they have composite boards. North Dakota is in the small group of states where the osteopaths do not have full practice privileges. At the present time there are five osteopathic schools in the United States, located in Des Moines, Ia.; Kirksville, Missouri; Kansas City, Missouri; Chicago, Illinois; and Philadelphia, Pennsylvania. The California College of Osteopathy became the California College of Medicine in 1964. A new osteopathic school is being proposed in Pontiac, Michigan. Some have found these schools favorable—some have not. In the last part of this report I put

in a definition concerning chiropractic. I put in facts and figures so that you would not be completely confused about chiropractic and osteopathy.

I think the osteopaths are going to get full practice privileges in North Dakota. The problems to be decided are:

1. Do we believe the D.O.'s practice scientific medicine?
2. Should they have full practice privileges?
3. Should there be a composite Board for examinations and licensure?

Speaker Christoferson directed this information to Committee No. 6 and charged the committee to present a resolution, with the guidance of Drs. Cleary and Nuessle, before the House on the following day for discussion and debate and action.

Secretary Buckingham was asked to read a letter received by Dr. Christoferson from Dr. G. Alfred Dodds, President:

SECRETARY BUCKINGHAM:

"Enclosed is a resolution from the Tennessee Medical Association which I am forwarding to you. You should read this Resolution over and consider either bringing it directly to the House of Delegates, or to the reference committee on Resolutions. Personally, I am wholeheartedly in favor of the resolution, and it may be that our society wants to instruct our AMA Delegate in this respect."

ss. G. Alfred Dodds, M.D., *President*

RESOLUTION
TENNESSEE MEDICAL ASSOCIATION

WHEREAS, the President's Committee on Heart Disease, Cancer and Stroke in December, 1964, published its comprehensive report including specific recommendations for the establishment of a national network of regional heart disease, cancer and stroke centers for clincal investigation, teaching and patient care in universities, hospitals and research centers and other institutions, and

WHEREAS, the President's Commission specifically recommended that 25 such centers for heart disease, 20 for cancer and 15 for stroke be established over a five year period in conjunction with major existing medical institutions plus an additional number of diagnostic and treatment stations to the number of 150 for heart disease, 200 for cancer and 100 for stroke plus another hundred for rehabilitation, and

WHEREAS, the President's Commission recommended additional programs including increased grant support of medical complexes, increased funds to the Public Health Service for establishment and maintenance of coordinated statewide laboratory facilities, the establishment of 25 bio-medical research institutes, an increased number of fellowships and investigatorships in clinical fields, increased funds to the Veterans Administration and Public Health hospital systems for training, research and patient care, and

WHEREAS, the President's Commission further recommended legislative changes in the Public Health Service Act by November 1, 1965, and new legislation regarding reorganization of federal programs as well as funding of federal programs, and

WHEREAS, the aims and ideals suggested by the President's Commission on Heart Disease, Cancer and Stroke are indisputably worthwhile although methods of implementation of such a vast program may be difficult on general agreement, and

WHEREAS, the effect of this new program upon existing institutions and resultant changes in the present structure of meeting the health needs of the population of the United States are of immediate concern to all members of the medical profession both in their professional roles and as citizens, and

WHEREAS, the body of practicing physicians at present do not appear to be aware of these proposals which will affect many phases of medical care in the United States today; now therefore be it

RESOLVED, that the Tennessee Medical Association through this House of Delegates take cognizance of the importance of these proposals and strongly recommend for the American Medical Association to vigorously study the large number of proposals in relation to their probable effect upon medical care and health problems in the United States, and be it further

RESOLVED, that the American Medical Association be requested to immediately study and cooperate in further discussion of this program during the entire period of its early development and later implementation by specific legislation, and be it further

RESOLVED, that the TMA delegates to the Americal Medical Association be instructed to introduce an appropriate resolution in the House of Delegates of the American Medical Association for the AMA to take steps to vigorously study and take appropriate action on all phases of this program, and be it further

RESOLVED, that copies of this resolution be immediately forwarded to all other state medical associations for informational purposes.

SPEAKER CHRISTOFERSON: I have here a letter from Dr. Donald McArthur to Dr. Ulmer regarding a Resolution from the Association of Minnesota Internists. You have a copy of this Resolution at your place and I would like to have you study this. I will refer this to Reference Committee, No. 4, for their study and action.

RESOLUTION OF THE
ASSOCIATION OF MINNESOTA INTERNISTS

WHEREAS, legislation is presently pending in the Congress of this nation which will, if passed into law, drastically affect the practice of medicine, and

WHEREAS, the overwhelming preponderance of practicing physicians in this country have indicated their dissatisfaction with some principles embodied in the aforesaid legislation, and

WHEREAS, the Association of Minnesota Internists embarked on a program of evaluation of national health legislation approximately 12 months ago for the purpose of proposing action on the part of organized medicine during 1965,

THEREFORE, be it resolved that the Minnesota State Medical Association encourage the American Medical Association to proceed with utmost diligence to formulate its own policy as to national health legislation, with such policy to embody all parts of the following recommendations which after careful study on a national level, are proven to be workable in solving the nation's health problems.

SPEAKER: There is an item of business, adopted by the Committee on Public Relations, September 27, 1964. This is a Code of Cooperation set forth as a guide to the physician in his relationship with the hospital, radio, TV and press, bearing in mind always the pressing obligation and responsibility of all doctors and hospital personnel in the welfare of the patient. The Code shall concern itself with the legal protection of all concerned groups, with the full individual rights of the patient being the foremost consideration at all times. This will be referred to Reference Committee, No. 2.

We now have four resolutions and I will ask the Secretary to simply state the essence of these resolutions, prior to their being referred to the Resolutions Committee for action.

SECRETARY BUCKINGHAM: We have two resolutions which are similar in nature, asking that resolutions be sent in far enough in advance so that they can be acted upon at the district level; otherwise no resolutions should be adopted except by a two-thirds majority vote of the delegates.

The next resolution deals with the termination of pregnancy prior to nine months.

The next resolution was submitted by the Third District Medical Society in regard to Chapter IV, Section II of the By-Laws. This resolution asks that an addendum to Section II, Chapter IV read as follows: "The number of delegates to be seated in the House of Delegates will be determined by the number of paid-up members as of December 31st of the previous year.

SPEAKER: All of these resolutions will be forwarded to Resolutions Committee, No. 6

We have two communications from the Council. Will the Secretary please read these communications?

SECRETARY BUCKINGHAM: The Council recommended that the House of Delegates authorize an Advisory Committee to be appointed, to the Safety Responsibility Division of the State Highway Department. This is in your Handbook on page 79, and also in a letter to Dr. Percy

L. Owens, Chairman of the Public Health Committee. This committee would give competent medical advice concerning physical and mental problems of persons operating motor vehicles in North Dakota. As a result of this competent medical advice, the Safety Responsibility Division of the State Highway Department would then be better able to judge and determine the physical and mental qualifications of a driver in granting, revoking, or refusing licenses to drivers.

The Council also referred to the House any action regarding a combined billing for AMPAC and COMPACT dues along with the regular Association dues.

SPEAKER CHRISTOFERSON: The communication from the Council regarding a Medical Advisory Committee for the State Highway Department's Safety Responsibility Division will be referred to Reference Committee, No. 4. Is there a recommendation regarding the size of this Committee, and how it shall be appointed? If so, this may be brought before the House tomorrow.

This situation regarding AMPAC and COMPACT in regard to billing on the regular statements will be referred to Reference Committee, No. 5, for their recommendations to be brought before the House tomorrow.

Any member wishing to present a matter to the House, should first present it to the proper reference committee for study and recommendation. I would prefer that these items be brought to the Reference Committee and acted upon by the Reference Committee and then brought before the House tomorrow for discussion and action.

Dr. Craven, I believe you have a check in your pocket and perhaps you would wish to present that check at this time.

DR. CRAVEN: This is one of the more pleasant duties of the President-Elect. I have here two sizable checks—one from the AMA Education and Research Foundation, signed by Dr. Blasingame for $4,283.49. This is North Dakota's Medical School's allotted portion of this fund. I understand that some of this check represents funds that have been ear-marked for the University of North Dakota Medical School.

The second check is one made out to Dr. Harwood from the North Dakota State Medical Association, office of Executive Secretary, in the amount of $500.00. This, as I understand it, is the Scholarship Fund.

DEAN HARWOOD: I would like to express my appreciation, and the appreciation of the faculty and students for this $500.00 check. This is one of the very fine scholarship awards, and we usually have a little affair when we present this.

The other check is one that comes to all Deans of all Medical Schools. This is a very precious fund. It is not subject to all the rules, regulations and red tape. This check is to take care of extra travel expense. The state funds takes care of the basic needs of the school, but not its total needs. This is a very precious check, and I thank all of you.

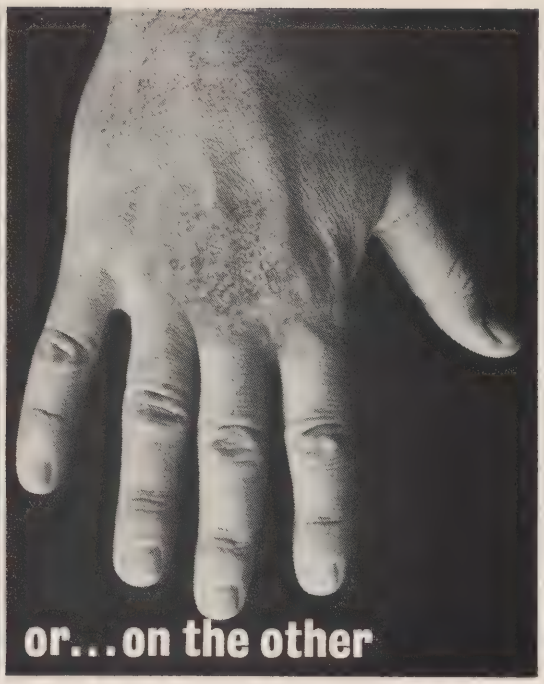
SPEAKER CHRISTOFERSON asked that each Chairman of the Reference Committees state the time and place of their meetings.

There being no further business, meeting was recessed by Speaker Christoferson until 2 P.M. on Sunday afternoon.

Recess at 5:00 P.M.

To be continued in the September Issue





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News Briefs . . .

North Dakota

DR. JAMES H. HOCKENBERRY opened a general medical practice in Oakes during July. He is now practicing in conjunction with Dr. Walter A. Craychee in the Oakes Clinic. Dr. Hockenberry received the M.D. from the University of Kansas.

* * * *

DRS. ALLEN R. NEUENSCHWANDER and DUANE D. GLASNER of Rolla recently purchased the Guenther Memorial Medical Center Building in Rolla and as of June 1 moved their practice, still known as the Rolla Clinic, to this new location. During July they were joined by a third physician, Dr. Arnold J. Overland, who for the past three years has conducted a general practice in Greenbush, Minnesota.

* * * *

DR. KENNETH N. AMSTUTZ, Minot internist, was recently elected president of the North Dakota Heart Association. Dr. Amstutz graduated in 1944 from the University of Michigan Medical School, Ann Arbor. He is a member of the American College of Chest Physicians and the American Society of Internal Medicine.

* * * *

DR. JOHAN A. ERICKSEN will assume the duties of radiologist at St. Alexius Hospital, Bismarck, in September. Dr. Ericksen was formerly with the department of radiology of the Quain and Ramstad Clinic, Bismarck.

* * * *

DR. VINCENT S. IRVINE, general practitioner in Lidgerwood for the past twenty-two years, received a fifty-year pin and certificate at the recent meeting of the North Dakota Medical Association. Dr. Irvine graduated in 1915 from the University of Manitoba Faculty of Medicine, Winnipeg. At age 76, Dr. Irvine is still in active practice.

Minnesota

Seven physicians from Minnesota, North Dakota, and South Dakota have been named to an eighteen-man committee which will study health manpower in these states under a $125,000 grant from the Hill Family Foundation, St. Paul. Purpose of the study is to assess the need for doctors, dentists, nurses, and paramedical personnel in the three-state area.

Physicians named are Drs. Victor Johnson, Mayo Graduate School of Medicine of the University of Minnesota at Rochester; Robert N. Barr, Minnesota Department of Health, Minneapolis; Herman A. Drill, Hopkins; Davitt A. Felder, St. Paul; Theodore H. Harwood, University of North Dakota School of Medicine, Grand Forks; Robert B. Howard, University of Minnesota Medical School, Minneapolis; and Chester L. Oppegaard, Crookston. Executive director of the committee is Dr. Osler L. Peterson, 1939 graduate of the University of Minnesota Medical School, and now on the staff at Harvard Medical School, Boston. The study is expected to be completed by November 1965. Findings will be published and distributed to interested persons and agencies by the Hill Family Foundation.

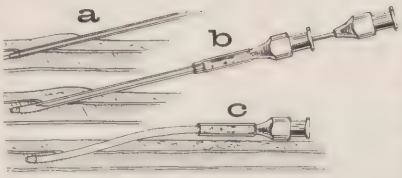
(Continued on page 18A)

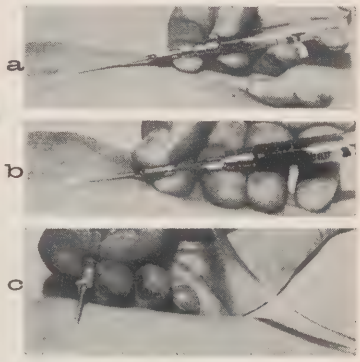
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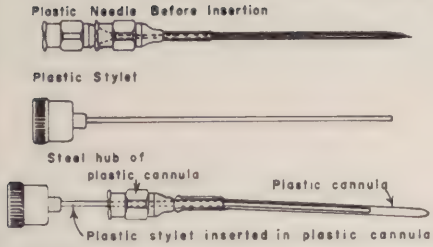




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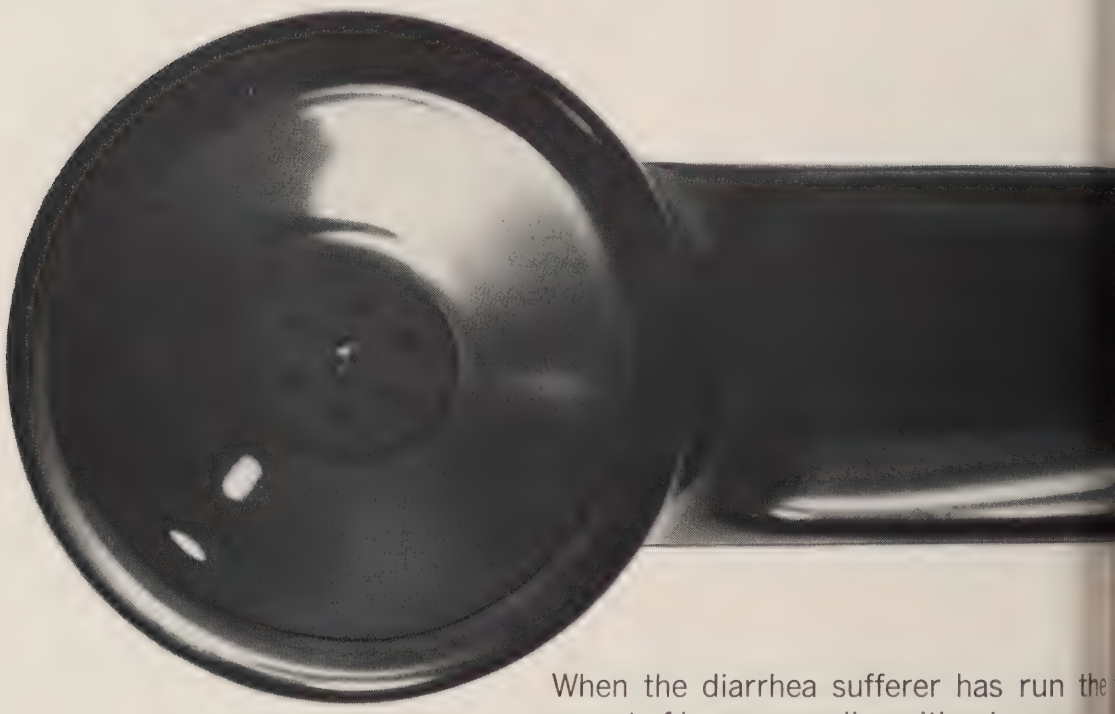
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NEWS BRIEFS

(Continued from page 14A)

EIGHTEN MINNESOTA PHYSICIANS who have each practiced medicine for fifty years received citations at the recent annual meeting of the Minnesota State Medical Association. Recipients were Drs. Arthur I. Arneson, Morris; Louis A. Buie, Sr., Rochester; Harry B. Clark, St. Cloud; Lloyd T. Davis, Wadena; Frank J. Elias, Duluth; Frederick W. Franchere, Lake Crystal; Walter H. Halloran, Jackson; Erling W. Hansen, Hopkins; Olga S. Hansen, Minneapolis; Fred Z. Havens, Rochester; Reuben A. Johnson, Minneapolis; Herman O. McPheeters, Minneapolis; Frank B. Mach, Minneapolis; Fredolph H. Magney, Duluth; Morton P. Morse, LeRoy; Edgar R. Sather, Alexandria; Charles W. Waas, St. Paul; and Clayton K. Williams, St. Paul.

* * * *

DR. HERMAN J. MOERSCH, emeritus head of a section of medicine in the Mayo Clinic, Rochester, has been awarded the gold medal of the American College of Chest Physicians for "meritorious service in diseases of the chest." Dr. Moersch was president of the college in 1956 and 1957.

* * * *

DR. EDWARD C. KENDALL, Princeton, New Jersey, who was chief of the laboratory of biochemistry of the Mayo Clinic, Rochester, from 1914 to 1951, has received the American Medical Association gold medal for scientific achievement and contributions to medical sciences. In 1950 Dr. Kendall and others were awarded the Nobel Prize in Physiology and Medicine for research on and partial synthesis of the hormones of the cortex of the adrenal glands.

DR. RICHARD J. SNYDER, obstetrician and gynecologist at the Mankato Clinic, has been certified as a diplomate of the American Board of Obstetrics and Gynecology. Dr. Snyder graduated from the University of Cincinnati College of Medicine in 1957.

* * * *

DR. W. ANDREW BUNTEN, from 1927 to 1929 a fellow in neurological surgery in the Mayo Graduate School of Medicine, University of Minnesota at Rochester, has been elected vice-president of the American Medical Association. Dr. Bunten now resides in Cheyenne, Wyoming. He graduated in 1922 from the University of Nebraska College of Medicine, Omaha.

* * * *

DR. CHARLES H. MAYO II, formerly a surgery fellow at Mayo Clinic, Rochester, and now doing research at the University of Minnesota Hospitals, Minneapolis, has been named to an 8-man advisory board by Concordia College, Moorhead. The board will advise the college in making long-range plans for its summer foreign language camps conducted each year in Northern Minnesota.

* * * *

DR. ARNOLD M. BERG, Roseau, has become associated with the Falls-Starekow Clinic in Thief River Falls. Dr. Berg graduated from the University of Minnesota Medical School in 1953 and practiced medicine in Roseau for the past ten years.

* * * *

DR. HAROLD J. SWAN has resigned his posts as cardiologist with Mayo Clinic, Rochester, and director of the cardiology laboratory of St. Mary's Hospital, Rochester, to become chief of cardiology at Cedars-Sinai Medical Cen-

(Continued on page 20A)

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NEWS BRIEFS

(Continued from page 18A)

ter, Los Angeles. Dr. Swan joined the Mayo Clinic staff ten years ago after serving more than three years as a research associate at the Mayo Graduate School of Medicine of the University of Minnesota at Rochester.

* * * *

DR. ROBERT P. BUCKLEY, Duluth periatrician, has been elected president of the Minnesota State Medical Association. Dr. Buckley is a member of the American Academy of Pediatricians and a 1929 graduate of the University of Minnesota Medical School.

Other officers elected are Drs. Harry B. Hall, Minneapolis, first vice-president; O. L. Norman Nelson, Minneapoils, second vice-president; Barnard Hall, St. Paul, secretary; Karl W. Anderson, Minneapolis, treasurer; John T. Pewters, Minneapolis, speaker; and Leon E. Steiner, Albert Lea, vice-speaker.

* * * *

DR. CLIFFORD F. GASTINEAU of the Mayo Clinic, Rochester, is one of 200 contributors and consultants for the book "Today's Health Guide," recently published by the American Medical Association. Dr. Gastineau is a member of the American College of Physicians, American Diabetes Association, the Endocrine Society, and the Central Society for Clinical Research.

* * * *

DR. HERBERT W. SCHMIDT, formerly a senior consultant in medicine at the Mayo Clinic, Rochester, and until recently associate medical director for Minnesota Mining and Manufacturing Company, St. Paul, has been appointed medical director to succeed Dr. William F. Hartfiel. Dr. Hartfiel will serve as a special consultant.

DR. LA RUE V. DAHLQUIST has joined Dr. Frank E. Boyd in the general practice of medicine at Pipestone. Dr. Dahlquist received his medical degree from the University of Nebraska in 1962. For the past two years he has been with the United States Public Health Service at Eagle Butte, South Dakota.

* * * *

DRS. ARNOLD O. SWENSEN, Duluth, and ORWOOD J. CAMPBELL, Minneapolis, have been awarded distinguished service medals by the Minnesota Medical Association, in recognition of their outstanding contributions to that organization. Both physicians formerly served as president of the state association, and both are now delegates to the American Medical Association.

* * * *

FOUR MINNESOTA PHYSICIANS have been elected members-at-large of the Minnesota Tuberculosis and Health Association. They are Drs. Ellen Z. Fifer, St. Louis Park; Dean S. Fleming, Minneapolis; John W. Lester, Mapleton; and R. Lawrence Thienes, St. Cloud. The Association has 25 members-at-large who assist in defining and implementing statewide programs of public education and prevention.

* * * *

DRS. ALTON C. OLSON and RICHARD E. ANONSEN, who have been working together in the general practice of medicine for the past ten years, recently opened new offices at Golden Valley in the Tyrol Medical-Dental Building.

* * * *

DR. JOHANNUS E. NORD, physician and surgeon, has opened an office in Ada for the general practice of medicine. Dr. Nord graduated in 1943 from Temple University School of Medicine, Philadelphia.



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NEWS BRIEFS

DR. JOYCE A. BICKFORD, Rochester State Hospital staff psychiatrist, has become chief-of-service for the day hospital at that institution, with medical responsibility for the preplacement section. Dr. Bickford succeeds Dr. Robert R. Rynearson, who is now psychiatric consultant to the geriatric wards.

* * * *

FIVE ST. PAUL AREA medical students are among 14 University of Minnesota freshmen who have been awarded $500 scholarships for the 1965-66 scholastic year from the Minnesota Medical Association. The award winners are Roger L. Gebhard, Ruth M. Geohle, Richard A. Wright, John W. Knott, and Richard M. Powell.

* * * *

DR. LAURENTIUS O. UNDERDAHL, Rochester, has been elected president of the American Diabetes Association. Dr. Underdahl is head of a section of medicine in the Mayo Clinic, Rochester, and associate professor of clinical medicine in the Mayo Graduate School of Medicine, University of Minnesota at Rochester.

* * * *

DR. DONALD MC CARTHY, St. Paul, deputy area medical director for the Veterans Administration, recently received a medal and an exceptional service certificate from the area VA directors. Dr. McCarthy will retire in the near future.

* * * *

DR. GLENN E. SCHROEDER, specialist in obstetrics and gynecology, has joined the staff of the Park Region Medical Center, Fergus Falls. A 1958 graduate of the University of Texas Southwestern Medical School, Dallas, Dr. Schroeder practiced for three years at Red Wing before coming to Fergus Falls.

* * * *

DR. WILLIAM H. RE MINE, head of a section of surgery in the Mayo Clinic, Rochester, and assistant professor in the Mayo Graduate School of Medicine, University of Minnesota at Rochester, has been awarded the honorary degree of doctor of science by the University of Richmond, Virginia.

* * * *

DR. HOWARD F. POLLEY, head of a section of medicine in the Mayo Clinic, Rochester, and professor of medicine in the Mayo Graduate School of Medicine, University of Minnesota at Rochester, has been awarded the honorary degree of doctor of science by Ohio Wesleyan University, Delaware.

* * * *

DR. DEWARD O. FERRIS, head of a section of surgery in the Mayo Clinic, Rochester, and professor of clinical surgery in the Mayo Graduate School of Medicine, University of Minnesota at Rochester, has been elected president of the Mayo Foundation chapter of Sigma Xi. Dr. Kendall B. Corbin was elected vice-president, and Dr. Alfred G. Karlson secretary-treasurer.

* * * *

DR. VICTOR E. SCHLOSSBERG, JR., specialist in internal medicine at Mankato Clinic, has resigned to enter practice at Mishawaha, Indiana. Dr. Schlossberg received his M.D. in 1955 from Indiana University.

* * * *

DR. HAROLD E. PAULUS has left the Austin Clinic to undertake a residency in internal medicine at the Veterans Administration Center General Medical and Surgical Hospital, Los Angeles, California.

(Continued on page 22A)

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WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

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MEDICAL DOCTOR—Medical Technology School desires doctor as a medical advisor. Write or phone Institute of Medical Technique, 1900 LaSalle, Minneapolis—Federal 3-3434.

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NEWS BRIEFS

(Continued from page 21A)

South Dakota

DR. PAUL H. HOHM, general practitioner and surgeon from Huron, has been elected president of the South Dakota Medical Association. Dr. John J. Stransky of Watertown is the new vice-president; Dr. Paul P. Brogdon, Jr., of Mitchell is the president-elect; and Dr. Robert H. Hayes of Winner is speaker.

* * * *

FIVE DOCTORS received annual awards at the recent meeting of the South Dakota Medical Association: Dr. Arthur P. Reding, Marion, the Distinguished Service Award; Dr. Alonzo P. Peeke, Volga, the Community Service Award; Dr. Robert H. Hayes, Winner, the Past President's Award; Dr. Myrtle S. Carney, formerly a South Dakotan but now a resident of Fort Worth, Texas, a fifty-year pin and certificate; and Dr. Harold F. Schuknecht, Boston otologist, the South Dakota Academy of Opthalmology and Otolaryngology Award.

* * * *

THREE GROUPS allied with the South Dakota Medical Association elected officers recently. The South Dakota Pediatric Society elected Dr. Harry W. Farrell, Sioux Falls, president; Dr. Willis F. Stanage, Yankton, vice-president; and Dr. Eberhard H. Heinrichs, Watertown, secretary-treasurer. The South Dakota Radiological Society elected Dr. Saul Friefeld, Brookings, president; Dr. Donald J. Peik, Sioux Falls, secretary-treasurer; and Dr. George F. Wood, Jr., Rapid City, counselor. Dr. John B. Slingsby, Rapid City, is the new president of the South Dakota Obstetrics-Gynecology Society; Dr. Granville H. Steele, Aberdeen, is vice-president; and Dr. Parry S. Nelson, Watertown, is secretary-treasurer.

* * * *

DR. WILLIAM O. HANSON, general practitioner, recently moved from De Smet to begin practice at the Huron Clinic. A native of Sioux Falls, Dr. Hanson received his medical degree from the University of Illinois in 1955. He is a member of the American Academy of General Practice.

* * * *

THE SOUTH DAKOTA MEDICAL ASSOCIATION recently donated $1,500 to provide a house for a physician in the town of South Dakota which is located in Chile, South America. Dr. Paul H. Hohm, of Huron, president of the State Medical Association, presented the donation to Chilean Ambassador Radomiro Tomic in behalf of all South Dakota doctors. Chile was torn by a severe earthquake earlier this year.



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Deaths . . .

DR. ARNOLD K. MYRABO, 48, pathologist at McKennan Hospital, Sioux Falls, South Dakota, since 1949, died June 2. A 1942 graduate of the University of Nebraska College of Medicine, Omaha, Dr. Myrabo was a member of the College of American Pathologists, the International College of Pathology, the American Society of Clinical Pathologists, and the staff of the University of South Dakota, Vermillion.

* * * *

DR. JALMAR H. SIMONS, 80, assistant professor at the University of Minnesota Medical School from 1919 to 1953, died June 6 in Minneapolis. Dr. Simons, who specialized in obstetrics and gynecology, received his medical degree from the University of Minnesota in 1910.

Book Reviews . . .

Traumatic Cervical Syndrome and Whiplash

by CHARLES W. GOFF, JOHN O. ALDEN, *and* JOHN H. ALDES, *128 pp., ill., J. B. Lippincott Co., Philadelphia, Pa., 1964. $5.00*

This book is intended to be a short compendium of the present knowledge concerning trauma to the cervical spine and its associated structures. On the whole it supplies this information rather well. The authors have decided that the use of the term "whiplash injuries" is quite acceptable; with this most orthopedic surgeons and neurosurgeons would disagree. The statement is also made that disability from neck injuries will largely disappear with termination of litigation; a debatable conclusion.

The text is divided into acute traumatic cervical syndrome, severe cervical trauma, and the chronic cervical syndrome. A chapter on treatment is necessarily brief but informative. Anatomy, physiology, and pathology are also discussed. There is a very short chapter on disability determination and another on posttraumatic neurosis.

This reviewer feels that this book contains a good deal of sound information in the 100 pages of its contents. An excellent list of references is also given.

It is a book well worth reading and rereading for the medical student, the general practitioner, and the specialist.

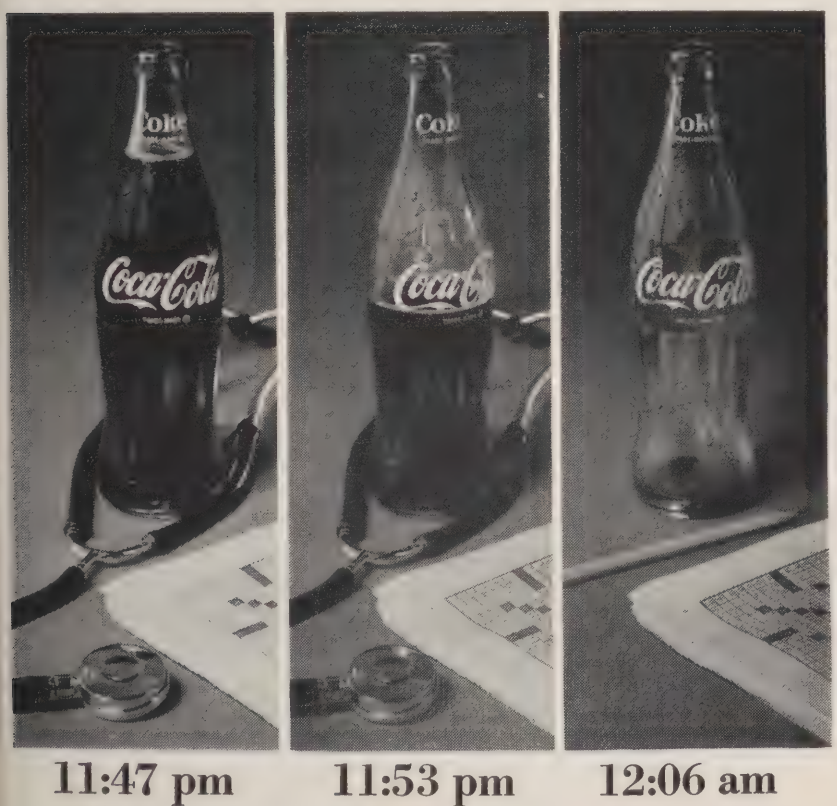
JOHN H. MOE, M.D.
Minneapolis

Sinoatrial Heart Block

by RICHARD J. GREENWOOD *and* DAVID FINKELSTEIN, *94 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $4.50*

This small book fills a gap in the large electrocardiographic literature. Only a few articles on sinoatrial block have been published, probably because it is considered to be clinically of little importance by the majority of cardiologists. According to the authors this view is not correct; in most published cases some cardiac pathology was present, and occasionally the sinoatrial block was the only manifestation. Thus, presence of sinoatrial block should alert the clinician and indicate of possible myocardiopathy or drug toxicity. The relation of sinoatrial block to other arrythmias, particularly the Wenckebach

(Continued on page 24A)



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(Continued from page 23A)

phenomenon, is thoroughly discussed. The sinoatrial block is not specific for any type of pathological condition, but this does not diminish its potential clinical importance.

However, the published cases are not a sound basis for evaluation in statistical terms, of the potential clinical importance, because the large majority of cases has not been published or most likely overlooked. In cases of sinus arrhythmia, as in most younger patients, "the diagnosis of block had best be forgotten." Thus, on the basis of published reports, the clinical significance may be overestimated. However, we agree with the authors that a reassessment of the clinical significance of sinoatrial block is needed.

The list of 229 references, going back to 1906, is exhaustive.

ERNST SIMONSON, M.E.
Minneapolis

Textbook of Otolaryngology

by DAVID D. DE WEESE *and* WILLIAM H. SAUNDERS, *2nd ed., 523 pp., ill., C. V. Mosby Co., St. Louis, Mo. 1964. $9.25*

The first edition of this textbook designed for medical students and general practitioners appeared in 1960 and promptly won acclaim. The second edition has been lengthened a little and some new illustrations have been added. The authors, who are prominent teachers and clinicians, have succeeded in producing a text that covers the field of otolaryngology exceedingly well from the standpoint of fundamentals, with emphasis on diagnosis and treatment. The book is adequately illustrated and many of the illustrations are photographs of high quality that faithfully illustrate a point or points.

An excellent first chapter on physical examination covers 33 pages, following which 140 pages are devoted to the throat, 90 pages to the nose, and 196 pages to the ear. In the content of the latter there is a special chapter on speech disorders. The final chapters, 31 and 32, are concerned with the salivary glands, cysts and other tumors of the head and neck, and related conditions.

This textbook can be highly recommended as an authoritative digest of practical information in the field of otolaryngology.

LAWRENCE R. BOIES, M.D.
MINNEAPOLIS

NEW BOOKS RECEIVED

Blood Program in World War II prepared and published under the direction of LEONARD D. HEATON, edited by JOHN BOYD COATES, JR., editor-in-chief, and ELIZABETH M. MC FETRIDGE, associate editor, 922 pp., ill., U.S. Government Printing Office, Washington, D.C., 1964. $8

Science and Psychoanalysis. Vol. VII, Development and Research edited by JULES H. MASSERMAN, 296 pp., ill., Grune & Stratton, New York City, 1964. $9.75

Diagnostic Medical Mycology by LEANOR D. HALEY, 204 pp., ill., Appleton-Century-Crofts, New York City, 1964. Paperback. $4.95

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Side effects: Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

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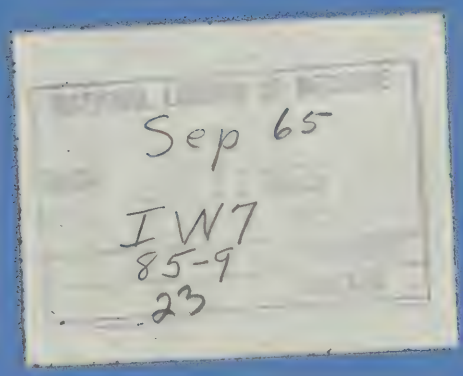
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Papaverine hydrochloride	16 mg.
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Phenylephrine hydrochloride	5 mg.
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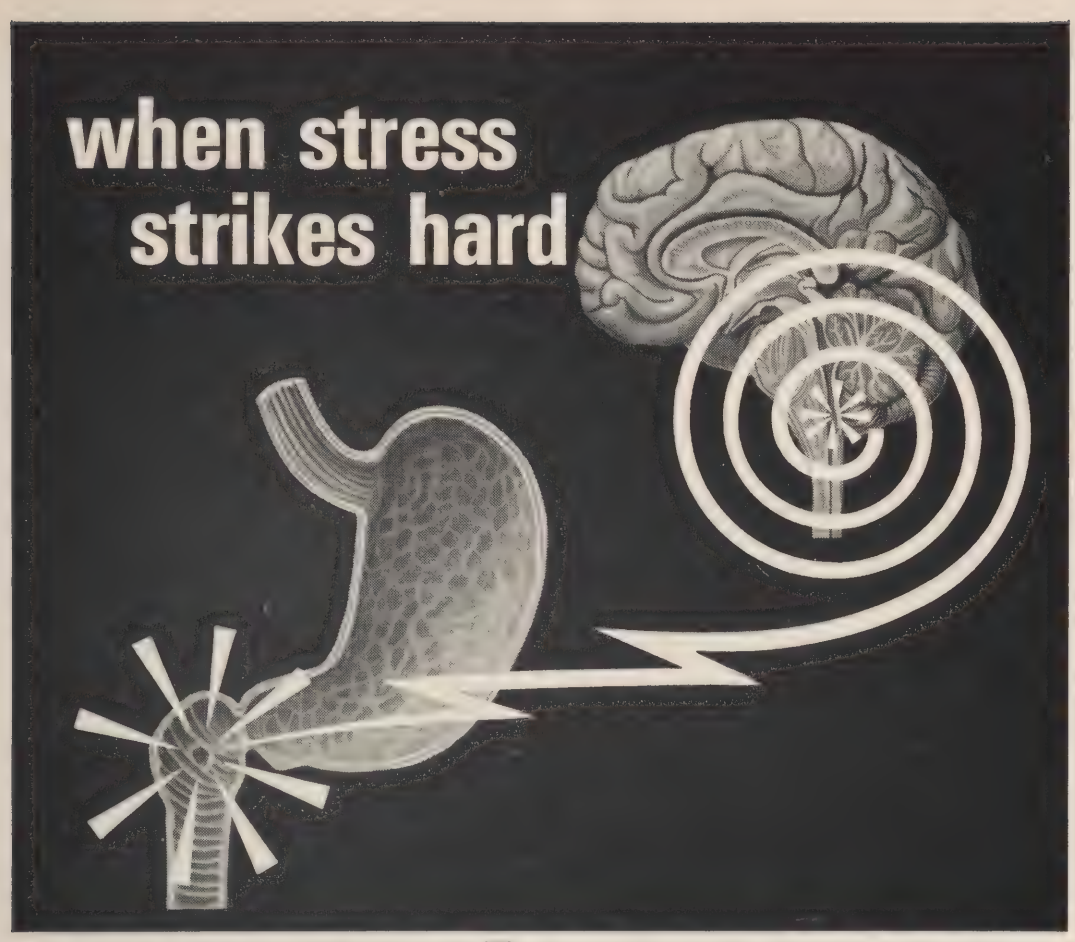
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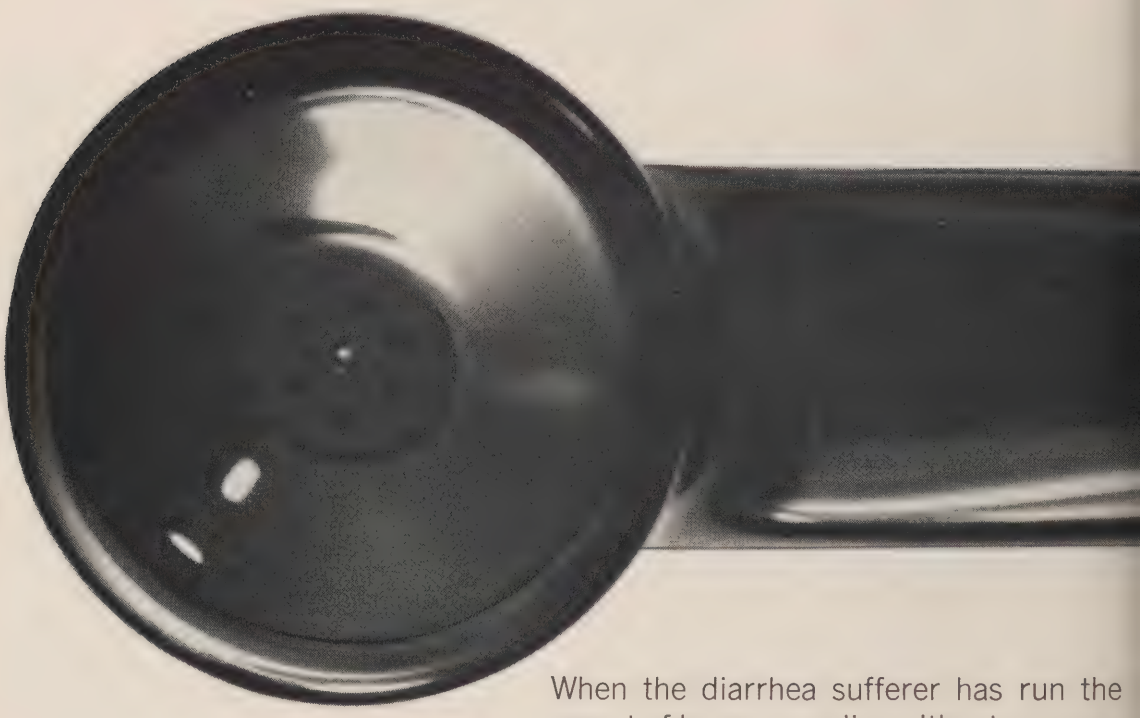
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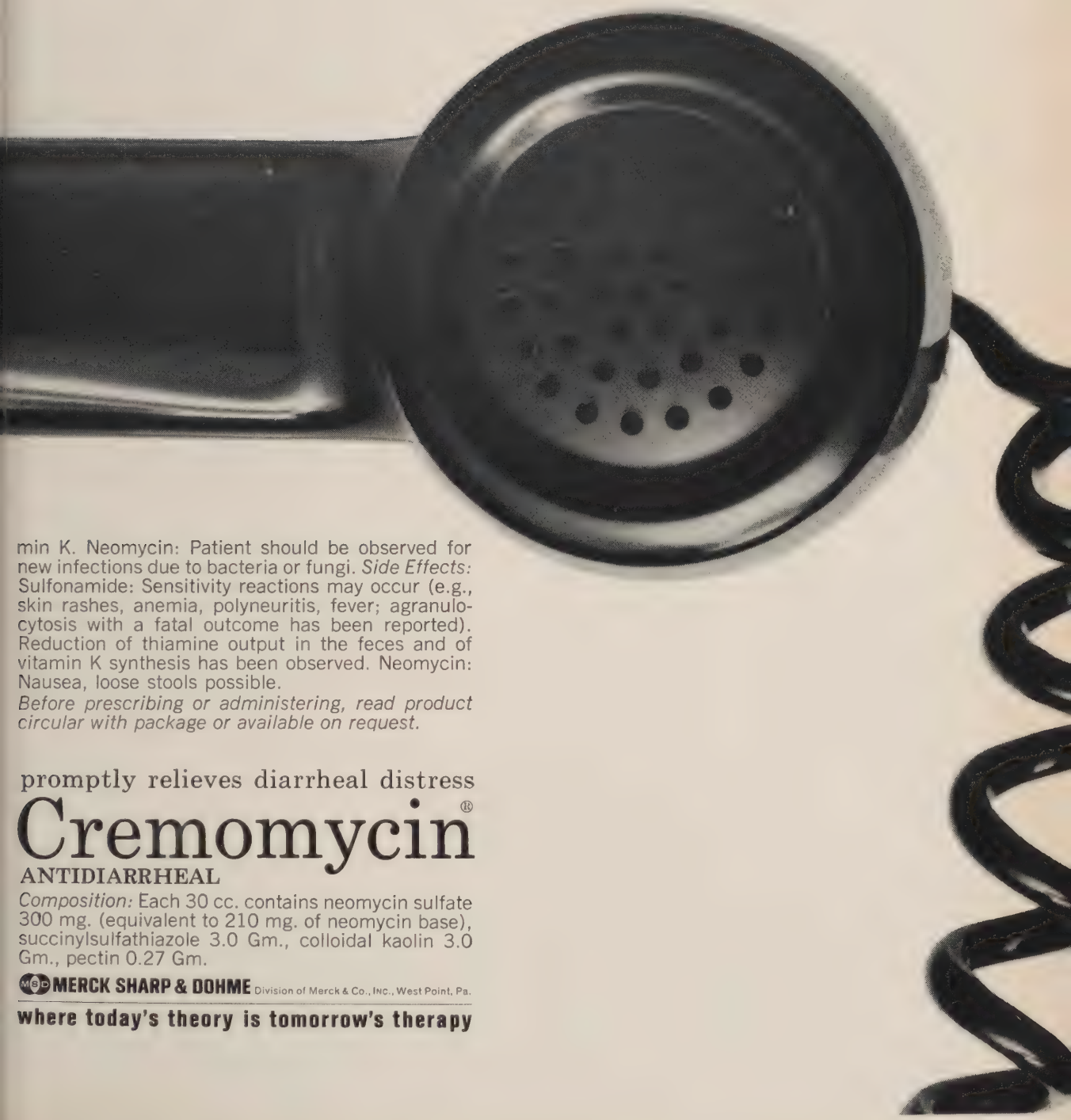


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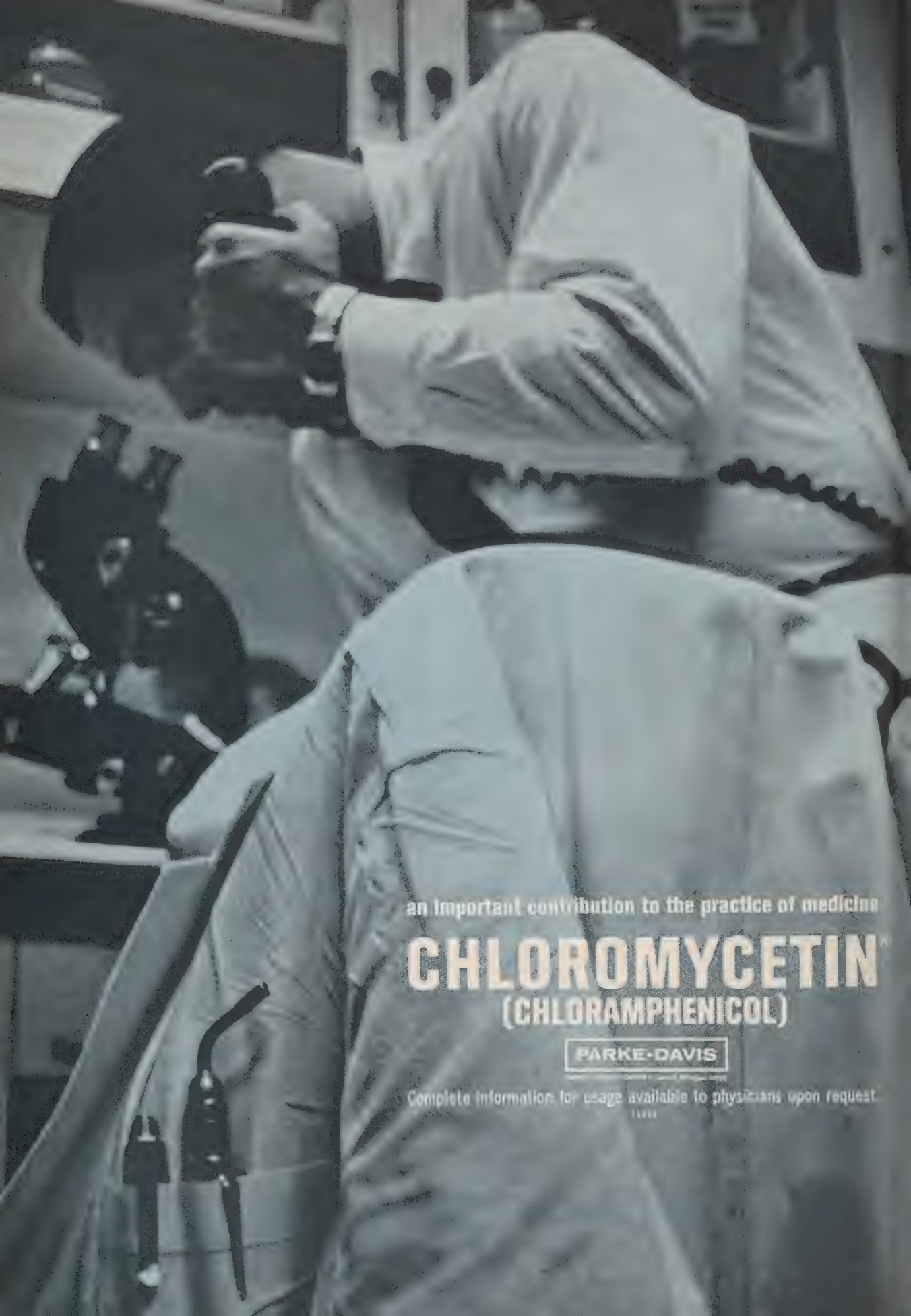
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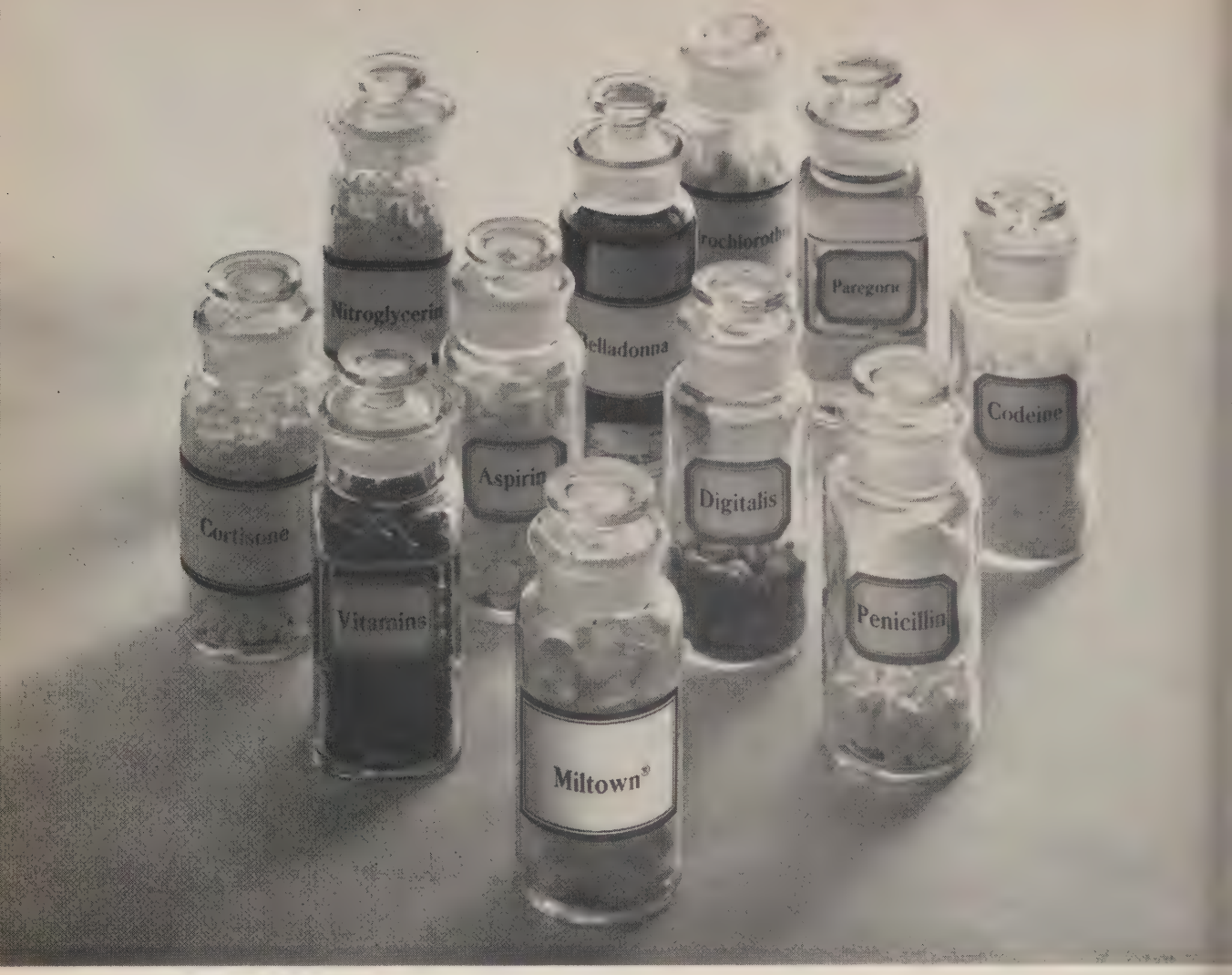
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Now it is well established that radioisotopes afford a convenient and reliable tool for visualization and evaluation of the function of various body organs. In his article, "Nuclear Medicine: Past and Present," in the October issue of THE JOURNAL-LANCET, Merle K. Loken, M.D., director of the Radioisotopic Clinic, University of Minnesota Hospital, reviews the progress that has been made, reports on the current status of nuclear techniques, and looks toward an increasingly important role for nuclear medicine in the medical evaluation of patients in the future.

In another important article, "Influence of Diet upon Nonfasting Blood Sugar and Glucose," E. Cheraskin, M.D., and W. M. Ringsdorf, Jr., D.M.D., of the University of Alabama Medical Center at Birmingham, reexamine the effects of a relatively low-refined carbohydrate, high-protein diet on nonfasting blood sugar and blood glucose levels and discuss possible clinical applications of the diet for nondiabetic disease states, particularly gout, multiple sclerosis, and atherosclerosis.

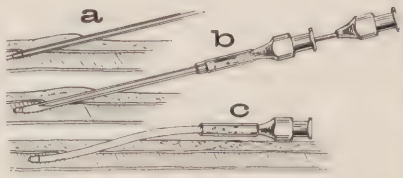
Dr. John S. Lundy, Seattle, editor of the "Section on Pain and Distress," features an article by Drs. Gibilisco, Goldstein, and Rushton of the Mayo Clinic on "The Differential Diagnosis of Atypical Facial Pain." A companion piece, "Pain of Dental Origin," by Drs. Raul Villarreal de la Garza and Maria Angelica Tamez de Villarreal of Monclova, Coahuila, Mexico, rounds out the subject.

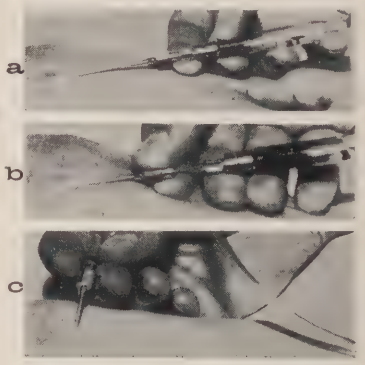
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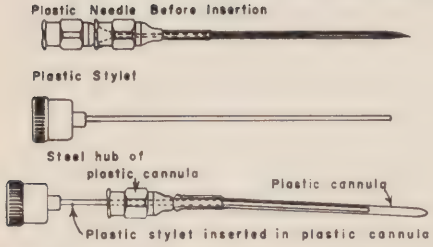




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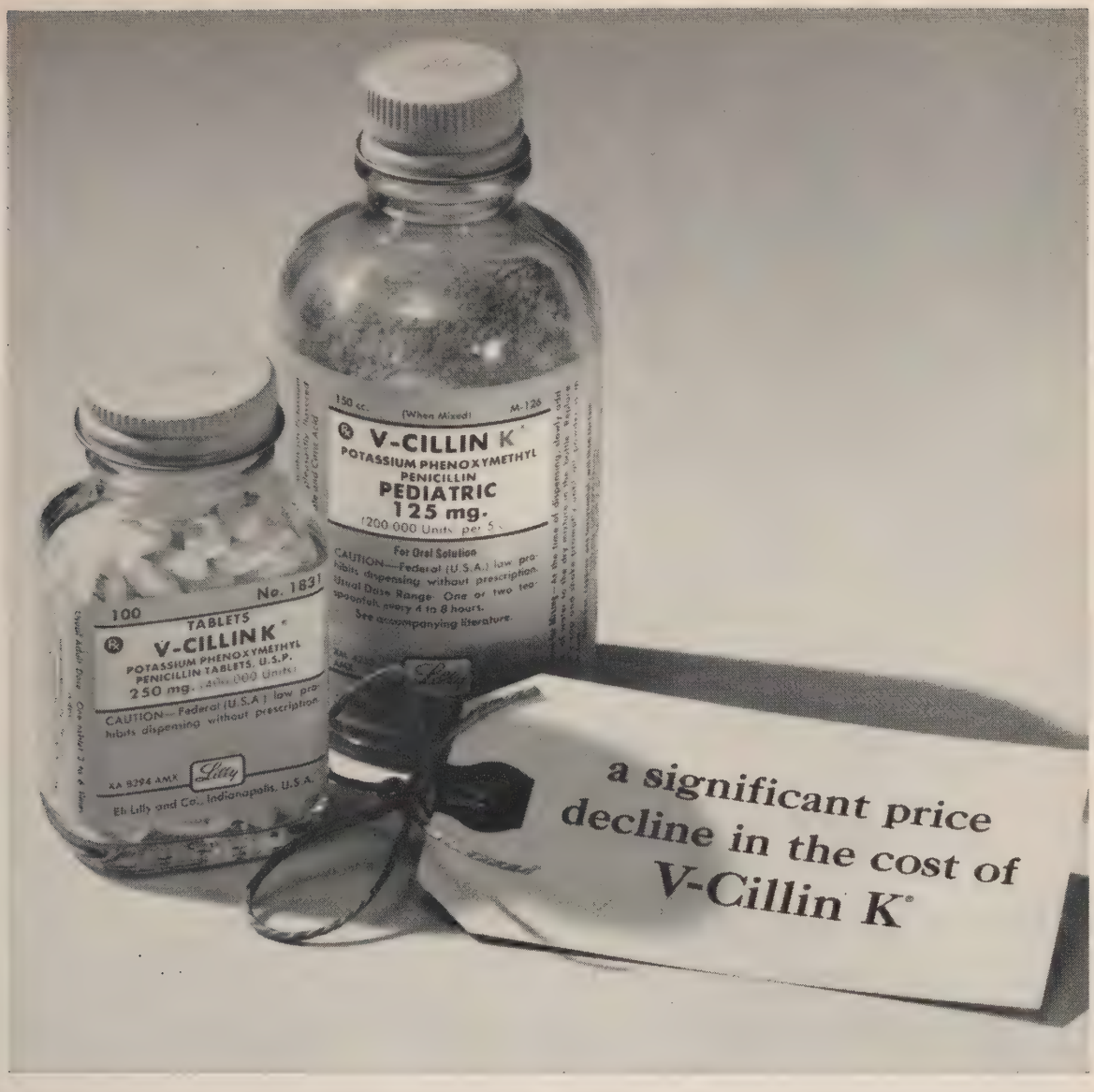
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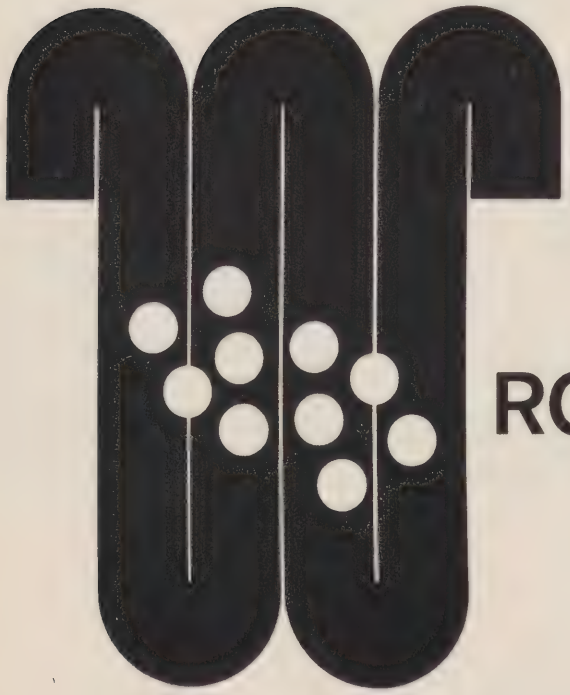
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A Simplified Approach for the Detection of Coagulation Disorders

WILLIAM KRIVIT, M.D., and JAMES G. WHITE, M.D.
Minneapolis

THROUGHOUT THE PAST years rapid developments in coagulation research have produced a burgeoning and complicated mass of information about the coagulation system in man.[1–4] The tumbling and twisting of names, numbers, and new concepts have led to a state of harried confusion for the unindoctrinated. As a result there is both anxiety in deciding whether a potential bleeder may proceed to surgery, as well as a disquieting frequency of postsurgical hemorrhagic disasters.

Whether or not a coagulation deficiency exists may be directly and simply ascertained by completion of the following:

A. Historical Review of the Patient's Personal and Family History
B. Laboratory Approaches
   1. Partial Thromboplastin (One Stage)
   2. Prothrombin Time (One Stage)
   3. Platelet Count (Direct Counts)
   4. Bleeding Time (Ivy)
   5. Tourniquet Test (Rumpel-Leede)
   6. Clot Retraction

HISTORICAL REVIEW OF PERSONAL AND FAMILY HISTORY

To ask a patient simply "Are you a bleeder?" is neither adequate nor reliable. A detailed history, carefully taken, is the single most important screening approach for determining the state of hemostasis.[5] This history must specifically include direct questions concerning possible blood loss following: circumcision, tonsillectomy and adenoidectomy, tooth extraction or loss of deciduous teeth, excessive bleeding or hematoma formation following trauma, and bleeding postoperatively. Any bleeding or hematoma formation that occurred or continued for twelve to twenty-four hours after any of the above should be cause for suspicion. If this bleeding has necessitated transfusion, then a coagulation disorder should be presumed to be present until proved otherwise.

To ascribe postoperative bleeding to inadequate surgical hemostasis is unwise and inappropriate. Bleeding postoperatively often occurs after certain types of surgery, particularly open heart, prostatic, or pulmonary surgery, but bleeding following an appendectomy, dental extraction, or tonsillectomy and adenoidectomy is unusual and demands investigation.

Of equal significance is the paradox of no bleeding following major surgery yet occurrence of hemorrhagic complications following minor trauma. This occurs in patients with well documented disorders. Epistaxis and abnormalities involving menstrual flow, because of their physiological nature and the wide variation in normal individuals, are not included in the above list. Yet questions concerning bleeding in these areas

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should form a part of the background information and must be evaluated concomitantly with other historical data.

A positive history is diagnostic of a coagulation abnormality, especially when unusual bleeding has been observed on more than one occasion.

Exhaustive laboratory study can reveal the nature of bleeding in practically every patient. Confirmation of the propensity to excessive bleeding, however, can be made in the vast majority of cases without recourse to an elaborate coagulation laboratory. A few readily available and relatively simple techniques will confirm the fact that abnormal hemostasis exists.

LABORATORY APPROACHES

Partial Thromboplastin Time (PTT). Over the past several years this test has become well standardized.[6,7] Complete kits containing all of the ingredients necessary for accurate determination of the PTT are available from several commercial sources. With a modicum of training the hospital laboratory technician or the physician can learn to run this test with ease and accuracy. The results of the PTT are particularly applicable to problems of the first stage of coagulation. Since the partial thromboplastin employed in the test is a phospholipid used as a substitute for platelets, the PTT will not uncover the presence of platelet abnormality.

An abnormality in PTT suggests a deficiency of one or more of the following factors.
Phase I

From patient's plasma { AHG VIII, PTC IX, PTA XI, Hageman XII } + "partial thromboplastin" from laboratory $\xrightarrow{Ca^{++}}$ Clot in 39-45 sec.

If other tests show that the patient's prothrombin time is normal, then the deficiency must be unrelated to Stuart Factor (X), Ac Globulin (V). For practical purposes, therefore, an isolated abnormality in the PTT in the presence of a normal prothrombin time is indicative of hemophilia. The commercially supplied kits for determining PTT also include specifically deficient substrate plasmas for comparison purposes. This makes the decision as to which type of hemophilia is involved not difficult. The assay procedures which determine the quantitative degree of deficiency of a specific factor require techniques beyond the scope of the average hospital laboratory.

The important principles in accurate utilization of the PTT test are to follow the outlines' procedure exactly, to take an adequate number of normal controls, and to do replicate determinations when an abnormality is found. The range of values for the normal PTT in one laboratory may not be exactly the same as in another. This is particularly true since many laboratories are now using the kaolin-modified PTT in which maximal contact activation shortens the time of normal considerably. In our laboratory, with the kaolin-modified PTT, the range in over 300 controls has been 39-45 seconds.

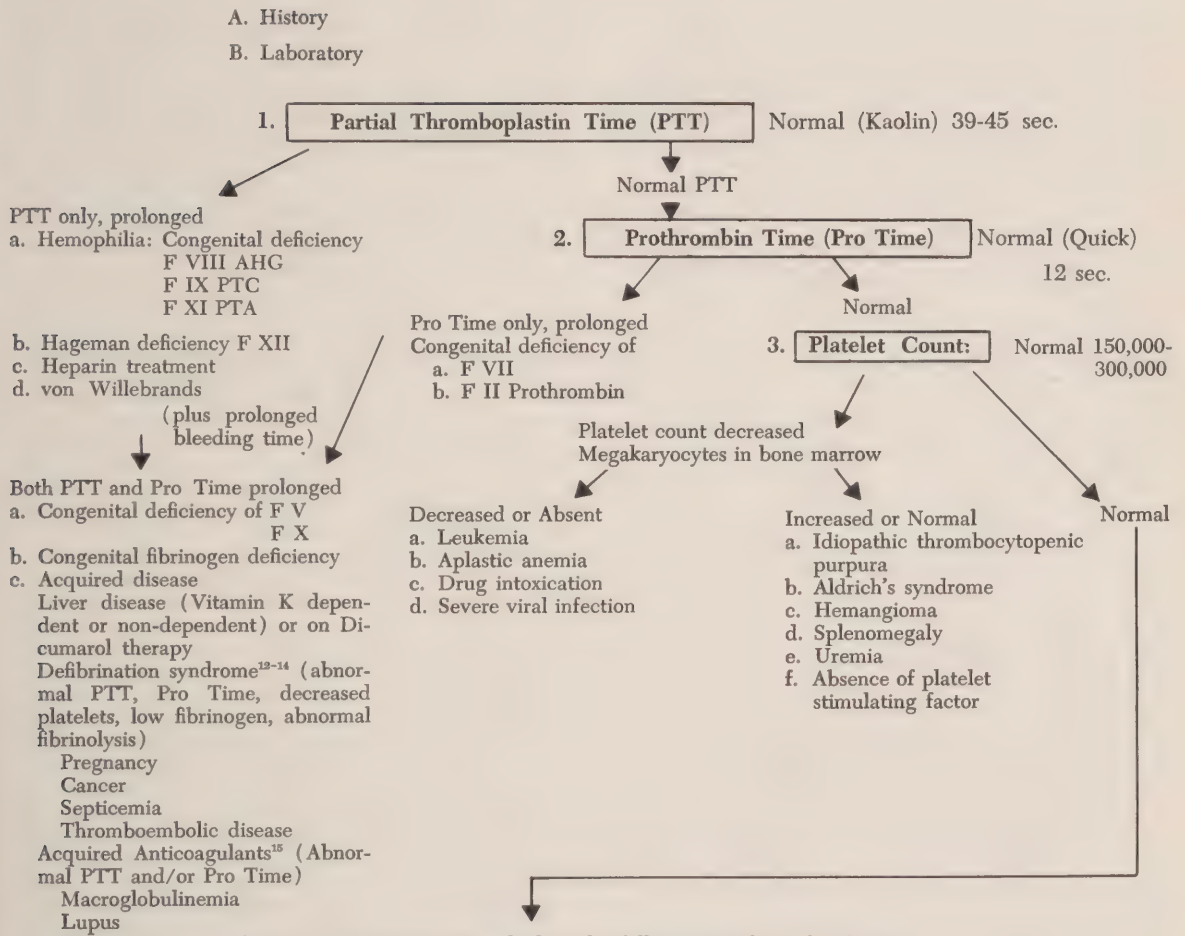
Prothrombin Time (One stage). This test originated by Dr. A. J. Quick has withstood the test of time. Reproducibility, simplicity, and sensitivity are its virtues. This test is similar to the PTT in that a phospholipid is substituted for the patient's platelets, and, therefore, will not detect platelet dysfunction. The phospholipid used in the prothrombin time is a more complete thromboplastin than that utilized in the PTT. The prothrombin time is insensitive to the hemophiliac factors for which the PTT is particularly adapted.
Phase II

From patient's plasma { Prothrombin II, S.P.C.A. VII, Ac Globulin V, Stuart Factor X, Fibrinogen I } + "complete thromboplastin" from laboratory $\xrightarrow{Ca^{++}}$ Clot in 12-13 sec.

Any deviation in the prothrombin time indicates an abnormality of the prothrombin complex. Specific assay will be required for the determination of the factor involved. Certain estimates, however, may be made on the basis of clinical knowledge and the results of other simple tests without resort to complicated assay procedures. A normal partial thromboplastin time in a patient whose prothrombin time is abnormal tends to eliminate factors V and X which affect the partial thromboplastin time. If the patient is known to have liver disease, then the likelihod is that he is deficient in the Vitamin K dependent factors (II, VII, IX, X) and treatment with Vitamin K may well alter the laboratory abnormalities If both the prothrombin time and partial thromboplastin time are abnormal, then it is suggestive that the patient is deficient either in factor X or factor V. If no clot forms at all in either the partial thromboplastin time or prothrombin time or if the clot is extremely friable when it eventually forms, then a state of hypofibrinogenemia or afibrinogenemia must be suspected.

The materials for the prothrombin time according to the procedure outlined by Dr. Quick are commercially available. Again, careful attention to the details of the procedure and determination of the large number of normal values for the particular laboratory are essential for proper

Is there a coagulation disorder?



This guide is constructed to allow the physician to confirm whether or not a coagulation defect is present and to suggest what the problem is most likely to be if a defect is detected.

If the PTT, prothrombin time, and platelet counts are normal, then a bleeding time, tourniquet test, and clot retraction should be ordered. An isolated abnormality in these latter tests indicates a platelet abnormality. Tests 7 through 11 are best performed in a sophisticated laboratory at present. When platelet function tests become more acceptable and become generally available, specific assay of platelet function will then be added.

evaluation of test results. A control plasma should be run daily if a large number of prothrombin time determinations are done in a hospital laboratory or, if this determination is performed infrequently, a normal plasma must be run simultaneously in every test.

Platelet Count (Direct Counting). An experienced technician looking at a properly prepared blood smear of a patient can usually estimate whether platelet numbers are adequate or not. However, when a question of hemostasis is involved an accurate platelet count is essential. The Brecher-Cronkite technique[8,9] with ammonium oxalate solution as the diluent is the easiest to prepare and therefore should be the most generally available technique. The limitation at the present time is the availability of phase contrast microscopes in all hospitals. The readiness with which light microscopes can be converted to phase contrast, however, should prevent this from being a continuing limitation. Determinating a normal range of platelet counts for the particular laboratory is also important. This will give the person doing the counts confidence in the method as well as establish normal ranges for the hospital.

Bleeding Time (Ivy). If the platelet count is low the bleeding time is an unnecessary procedure, since the bleeding time will almost always be prolonged in this situation. The Duke and Ivy methods are both useful in detecting abnormalities of the bleeding time. Of the two, the Ivy is the most useful in determining the presence of a prolonged bleeding time, and the Duke method more useful in determining response to therapy with plasma.[10] Choice of one of the two techniques and standardization of method are recommended for use in a laboratory. When this is done reliable results will be achieved.

A prolonged bleeding time test is not indicative, by itself, of a vascular abnormality. Rather the deficiencies in cutaneous hemostasis are more related to platelet dysfunction or to deficiencies in plasma factors involved in cutaneous bleeding.

Tourniquet Test (Rumpel-Leede). This test is not needed as a screening method if the platelet count or bleeding times are abnormal. Yet there have been times in which the abnormal cuff test has been the only abnormality of the coagulation mechanism present. Also, it is easily performed by the physician himself and therefore involves him directly in the evaluation of hemostasis in his patients. A positive cuff test should serve only as an impetus to further study despite the apparent normalcy of the rest of the screening tests.

Clot Retraction. If thrombocytopenia is evident then it is unnecessary to perform clot retraction which will certainly be abnormal. But if the platelet count is normal and there is a history of bleeding, then clot retraction is an essential part of the evaluation of platelet function in the patient with a suggestive bleeding history. This test is simply performed by a number of procedures. It is well to remember, however, that the procedural steps must be followed exactly for reliable results especially with regard to the preparation of the tubes used for the clot retraction determination. The test tubes should be chemically clean and heated shortly before use.

The Lee-White clotting time has been removed from this schema for a laboratory approach to a possible hemostatic disorder. A clotting time performed by the Lee-White method is singularly unable to detect disorders of hemostatic function.[11] A normal Lee-White does not rule out hemophilia and is, therefore, of no value as a screening test.

Supported by grants from the American Cancer Society, Minnesota Division, and USPHS No. AM-02917-05.

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Some Present-Day Problems in Infectious Heart Disease

JOSEPH E. GERACI, M.D.

Rochester, Minnesota

IN THIS REVIEW I shall confine my remarks to certain aspects of bacterial endocarditis, infections of the pericardium, the antibiotic treatment and prophylaxis of beta-hemolytic streptococcal infections and rheumatic fever, and finally the antibiotic prophylaxis of bacterial endocarditis.

BACTERIAL ENDOCARDITIS IN GENERAL

I shall speak only briefly of bacterial endocarditis inasmuch as we are currently reviewing the data on 200 patients seen in the seven-year period January 1958 through December 1964. These data subsequently will be presented in separate communications and compared with data already published on 172 patients seen in the seven-year period January 1951 through December 1957. A preliminary review of this second period indicates that the incidence of bacterial endocarditis has remained as high as in the first period, or perhaps slightly higher, particularly in the last two years of the second period. Thus, the incidence has not continued to fall as might have been expected with the continued widespread use of antibiotics. The table gives a breakdown of the cases by type of valvular infection for the 2 periods.

The proportion of infections due to penicillin G-sensitive streptococci has fallen to less than 50% for the second period. The proportion due to enterococci has also decreased so that streptococcal infections represent 58% of the second group, whereas before 1951 these infections represented 90 to 95% of all cases.

Staphylococcal infections, however, have definitely increased. Gram-negative infections also have increased although this is not apparent from the table. There the 6% given for the first period are misleading since most of the patients in this category were seen at one time as a result of Pseudomonas contamination of temporarily inadequate sterilization of the heart-lung machine. If these cases were eliminated from the first group, the proportion of infections due to gram-negative bacteria would have been closer to 2 or 3%. This same change in the etiology of bacterial endocarditis has been noted by other authors recently. There has also been an increase in fungal infections, particularly in postoperative cardiac patients.

Because of the decrease in infections caused by antibiotic-sensitive organisms and the increase in those caused by antibiotic-resistant organisms and because delay in diagnosis with delay in adequate antibiotic therapy results in increased morbidity and mortality, I would emphasize the need for early diagnosis and early appropriate bactericidal antibiotic therapy. Only in this way can the present persisting high morbidity with resultant complications and high mortality be reduced.

TABLE

DISTRIBUTION OF CASES OF BACTERIAL ENDOCARDITIS BY TYPE OF VALVULAR INFECTION FOR 2 PERIODS

Type of infection	*1951-1957 (172 cases)*	*1958-1964 (200 cases)*
	percent of cases	
Streptococcus mitis or "viridans"	53	49
Enterococcal	16	9
Staphylococcal	16	28
Gram-negative bacterial	6	5
Negative blood culture	8	7
Miscellaneous	2	2

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For this reason, individuals with a heart murmur should be thought of as having bacterial endocarditis when they get sick. Only alertness to the possibility that the patient may have such an infection will make early diagnosis possible. Blood cultures should be taken before any antibiotic therapy is given; they are necessary for precise diagnosis and appropriate bactericidal therapy. The administration of antibiotics for fever, respiratory infections, or mild indeterminate illnesses often renders the diagnosis of bacterial endocarditis difficult and complicates the problem of appropriate therapy. Early precise diagnosis, in the first two to four weeks of illness, with adequate treatment almost always permits cure of bacterial endocarditis, whereas delay and improper treatment result in prolonged morbidity and high mortality.

The clinical features of bacterial endocarditis are usually some or all of the following: (1) symptoms and signs of systemic infection with fever, (2) evidence of heart disease with the presence of a murmur, (3) bacteremia with positive blood cultures, and (4) embolic phenomena in various organs and the extremities.

The clinical picture varies from that of the relatively asymptomatic patient with little or no fever and with a minimal hemodynamically insignificant murmur, to that of the acutely ill patient with rapidly fulminating infection who may die within several days of onset of the infection, especially if it is staphylococcal. Bacterial endocarditis, like tuberculosis and syphilis, is remarkably protean in its manifestations. It may imitate almost any clinical syndrome or disease since almost any body system may be predominantly involved. Unless the physician thinks of it constantly whenever a diagnosis is not readily apparent, the diagnosis will be missed or considerably delayed. In most instances the combination of nonspecific symptoms of ill health or infection plus fever and a heart murmur should lead the physician to suspect the diagnosis and to get several blood cultures before he begins any form of antibiotic therapy.

Rarely, fever or a heart murmur, but almost never both, is lacking in bacterial endocarditis. This infection should be thought of even in the absence of fever or the systemic manifestations of a febrile illness in an individual, especially an elderly one, with an apparently unimportant, minimal, hemodynamically insignificant murmur. Endocarditis should also be thought of in patients with obscure anemia; in those with obscure disease of the central nervous system such as meningitis, subarachnoid hemorrhage, or multiple focal areas of brain involvement; in those with obscure renal insufficiency; and in cardiac patients who suddenly do poorly and develop congestive heart failure when they have been doing well previously. Careful postoperative observation is necessary to uncover endocarditis in patients who have had bypass operations on the heart.

I shall not discuss the many details of antibiotic management of the many forms of bacterial endocarditis. Suffice it to say that a bactericidal antibiotic or a bactericidal combination of antibiotics should be employed for optimal therapeutic results. Optimal treatment requires the following: (1) early diagnosis with precise identification of the causative organism and the determination of its in vitro sensitivity, that is, the minimal concentration of antibiotic that inhibits the organism and the minimal concentration that kills it, (2) early initiation of appropriate bactericidal antibiotic treatment, (3) guidance of therapy by means of a serum bactericidal test to ensure that a bactericidal regimen is used, (4) adequate rest in bed during treatment, at least initially, (5) adequate observation during treatment for side effects and toxicity of the drug and for detection of focuses of infection, and (6) adequate follow-up for three months to detect post-treatment complications, embolic episodes, and relapses.

ENDOCARDITIS DUE TO PENCILLIN-SENSITIVE S. MITIS OR "VIRIDANS"

My colleagues and I continue to treat this group with a two-week regimen. Initially we used 1 million units of aqueous procaine penicillin G and 1 gm. of combined streptomycin-dihydrostreptomycin every twelve hours intramuscularly, together with probenecid (Benemid®), 0.5 gm. orally every six hours for fourteen days, with successful results and minimal side effects and toxicity. Our results were comparable to, if not better than, those obtained by others with aqueous crystalline penicillin G alone injected intramuscularly at frequent intervals around the clock for four to six weeks. Because dihydrostreptomycin occasionally caused delayed hearing loss, it was removed from all combinations of antibiotics and from the market.

Thereafter, from 1959 through 1963, we used 2 gm. of streptomycin per day in the above described regimen. With this dosage of streptomycin, the incidence of eighth nerve vestibular involvement, 25% of 60 patients, was increased sharply. At times, marked reactions occurred toward the end of the first week of therapy.

At present, we are investigating clinically 2 slightly different two-week regimens. One regi-

men employs 10 million to 20 million units of aqueous crystalline penicillin G given by continuous intravenous drip and 0.5 gm. of streptomycin given intramuscularly every twelve hours together with Benemid®. The other regimen employs 1 million units of aqueous procaine penicillin G and 0.5 gm. of streptomycin each given intramuscularly every eight hours together with Benemid®. These regimens appear promising. Intramuscular injection would seem preferable to avoid the risk of staphylococcal superinfection from the indwelling needle required in continuous intravenous therapy. Nine out of 10 patients are able to take Benemid® without side effects or toxicity and it should be used to enhance penicillemia and the bactericidal effect.

In patients allergic to penicillin G, it appears that cephalothin or cephaloridine and streptomycin in combination may be an adequate bactericidal substitute. The use of a combination of erythromycin and streptomycin for a longer period of three to four weeks has proved of value in the past. For many reasons we continue to use parenteral treatment for bacterial endocarditis even though a number of competent observers have demonstrated that oral therapy gives equally good results.

ENTEROCOCCAL ENDOCARDITIS

Long-term treatment of four weeks with aqueous crystalline penicillin G in large doses and streptomycin and Benemid® in combination should be used for enterococcal endocarditis. We begin with 20 million units of penicillin G given by continuous intravenous drip plus 0.5 gm. of streptomycin given intramuscularly every twelve hours. Smaller doses of streptomycin are given if renal function is impaired. Benemid®, 0.5 gm., is given orally every six to eight hours to enhance the effect of the penicillemia. A serum bactericidal test is then done one hour after the first injection of streptomycin; if the bactericidal effect occurs in a 1 to 4 dilution of the patient's serum the regimen is continued; if the bactericidal effect occurs in a lesser dilution the dose of penicillin G is increased in amounts of 20 million units until a total killing effect in a 1 to 4 dilution of the patient's serum is obtained.

Patients allergic to penicillin G have to be desensitized or hyposensitized. In a few instances another antibiotic agent alone or a combination of antibiotics can successfully replace the penicillin G-streptomycin-Benemid® regimen in these patients.

We have not found ristocetin effective and do not use it. We consider it a bacteriostatic agent. In 6 patients given 3 and 6 gm. of the drug per day at the start of therapy, neither the serum assays for ristocetin nor the serum bactericidal tests gave adequate results. In all 6 patients the minimal bactericidal concentration of ristocetin for the enterococcus was higher than the ristocetin serum levels obtained with both the 3 and the 6 gm. dose. In none of the group did the serum bactericidal test show any bactericidal effect, even in undiluted serum, with either dose.

The minimal bactericidal concentration of penicillin G for the enterococcus should be determined in all instances. The enterococcus isolated in our last 2 patients was killed by concentrations of 5 to 10 μg. per milliliter of penicillin G and this antibiotic alone gave adequate killing effect in the patient's serum as determined by the serum bactericidal test. Both patients were successfully treated with penicillin alone rather than with the combination. This is of particular importance in patients who have significant renal insufficiency or who have had or develop early eighth nerve toxicity.

STAPHYLOCOCCAL ENDOCARDITIS

The treatment of coagulase-positive or coagulase-negative staphylococcal endocarditis depends on the sensitivity of the organism to penicillin G. If it is sensitive to 1 μg. or less per milliliter, this is the agent of choice. Depending on the degree of sensitivity, penicillin G may be given alone intramuscularly and intermittently in modest dosage or in larger doses by continuous intravenous drip without or with Benemid®. The aim is to achieve an adequate bactericidal effect in a 1 to 4 dilution of the patient's serum with the regimen used.

When the staphylococci are resistant to penicillin G, requiring more than 1 μg. of the agent per milliliter for inhibition, methicillin (2, 6-dimethoxyphenyl penicillin), one of the new semisynthetic penicillins, is the agent of choice. The minimal regimen in patients who are not very sick is 1 gm. given intramuscularly every three hours around the clock, totaling 8 gm. per day, for at least a month. When the patient is very sick, much more than this is used initially; we usually give 1 gm. intravenously and 1 gm. intramuscularly every two or three hours, totaling 16 to 24 gm. per day, until the infection is under control. Then a dose of 1 gm. every three hours may be substituted until the end of the treatment period. Benemid® may also be used in combination with methicillin to increase the penicillemia and to reduce the dose and cost of methicillin.

The status of the other penicillinase-resistant semisynthetic penicillins in the therapy of staphy-

lococcal endocarditis remains to be carefully evaluated. Our results with methicillin therapy have been as good as those with vancomycin. We are now fully evaluating our experience with the above described regimen and we shall report on it in detail soon. Postoperatively in patients who have undergone cardiac bypass procedures, when the infection involves a foreign-body prosthesis or unabsorbable suture material, treatment with any bactericidal antistaphylococcal agent or agents in any amount has generally not been successful until the foreign material has been removed. In these patients, as soon as the diagnosis is suspected, the intense regimen mentioned above is started and kept up for one month if the patient does well. If the patient does not do well or relapses during therapy or immediately after suspension of therapy, reoperation should be considered.

When the patient is allergic to the penicillins and cannot take them, cephalothin or cephaloridine is the second antibiotic of choice. The optimal regimen has yet to be worked out, but the usual dose is 1 gm. given parenterally every three or four hours. Clinical experience with cephalothin and the latest cephalosporin derivative, cephaloridine, in the therapy of bacterial endocarditis is meager. If the patient cannot take cephalothin (I have seen a severe, widespread urticarial eruption following the first injection of cephalothin, 1 gm. intramuscularly and 1 gm. intravenously given simultaneously, in a patient allergic to penicillin G), then vancomycin is the antibiotic of third choice; this is given intravenously in doses of 1 gm. every six hours at first (but not by continuous intravenous drip) until the infection is under control, and then it is given in doses of 1 gm. every twelve hours for a total treatment period of four weeks.

Gram-negative bacterial endocarditis, bacterial endocarditis without positive blood cultures, and fungal, rickettsial, viral, and miscellaneous forms of bacterial endocarditis will be considered in subsequent publications.

BACTERIAL PERICARDITIS

Suppurative pericarditis. The incidence of purulent pericarditis has decreased markedly since antibiotic therapy was introduced. With modern antibiotic agents, infections rarely progress to the state where suppurative pericarditis occurs. However, purulent pericarditis remains an important entity because it can be overlooked so easily, because symptoms of it are masked readily by antibiotic therapy, and because it is beginning to reappear as a result of the emergence of staphylococci and other organisms resistant to antibiotics. Before the antibiotic era, this disease carried a high mortality rate and the only therapy available was surgical.

Purulent pericarditis usually occurs at the height of an associated illness; rarely it may be the only illness, as when it is a complication of an open-heart operation. In the past it usually followed extensive pneumococcal pneumonia with bacteremia in which early treatment was neglected. Other diseases that may cause purulent pericarditis are acute bacterial endocarditis, osteomyelitis, stab wounds, puerperal sepsis, genitourinary infections, and septicemias arising from other disease states. The most common pathogens involved today are the staphylococcus particularly and the pneumonococcus, the streptococcus, and the meningococcus to a lesser extent; in children Hemophilus influenzae is the most common cause. These organisms reach the pericardium by direct extension from the lung, pleura, or mediastinum, by the bloodstream or through stab wounds, or by direct introduction into the pericardium at the time of an open-heart operation.

The diagnosis of purulent pericarditis rests primarily on thinking of it as a possibility plus one or more of the following signs and symptoms: a rapid paradoxical pulse, fever not adequately explained when the initial infection seems to have been under control, dyspnea and cyanosis that cannot be adequately explained, precordial distress, a pericardial friction rub, an increase in the cardiac outline, engorgement of the neck veins, distant heart tones, and electrocardiographic changes. When the diagnosis is suspected, a pericardial tap should be done at once. This is the only way to make a precise diagnosis.

Once the diagnosis has been made, treatment depends on the stage of development of the disease. If the diagnosis is made early, in the serous or the serofibrinous stage, intensive systemic appropriate antibiotic therapy together with instillation of antibiotics into the pericardial cavity may be curative. When pus has formed, one may attempt to eradicate the infection by "medical debridement," for example by repeated aspirations of the pus and the instillation of the appropriate antibiotic or combination of antibiotics and the enzymes streptokinase and streptodornase into the pericardial cavity. These enzymes can be used in the pericardium without untoward effects. If the purulent fluid is too thick to aspirate, open surgical drainage is necessary.

More recently, a number of authors have expressed the view that surgical drainage is indicated as soon as the diagnosis is made. Drainage

may be accomplished by repeated pericardiocenteses if the fluid is thin, if aspiration is accomplished easily, and if adequate relief of tamponade is obtained. Pericardiostomy, on the other hand, is recommended in patients with recurrent tamponade, when the fluid is thick and aspiration is difficult.

The choice of antibiotics for systemic therapy depends on the causative organism and the results of in vitro sensitivity tests. The limited data on diffusion of antibiotics into pericardial fluid indicate that most of the antibiotics get into the pericardial fluid in adequate amounts but probably not enough to cure purulent pericarditis, particularly in the later stages of the disease. The choice for local instillation into the pericardial cavity should be restricted to the bactericidal agents such as the penicillins, vancomycin and kanamycin, streptomycin, bacitracin, neomycin, polymyxin or colistin, and the cephalosporins.

Inasmuch as purulent pericarditis has become largely a hospital-acquired antibiotic-resistant staphylococcal infection, one should perhaps commence antibiotic therapy with large doses of methicillin given parenterally into the pericardial cavity (50 to 100 mg.) when the diagnosis is first entertained after cultures of the blood and pericardial fluid have been obtained. One gram of methicillin should be given intramuscularly every three hours as a minimum. In acutely ill patients and those whose blood cultures are positive for staphylococci, larger doses should be given initially: 1 gm. intravenously and 1 gm. intramuscularly every two or three hours until the infection is under control; the dose can then be reduced to a maintenance level of 1 gm. given every three hours intramuscularly.

When the culture reports and in vitro sensitivity data become available, the antibiotic regimen can be changed as necessary. For penicillin G-sensitive staphylococcal infections and for infections caused by pneumococci, streptococci, and meningococci, large doses of 20 million units of intravenously administered penicillin G may be given alone since these organisms remain uniformly sensitive to this agent. For a gram-negative bacterial infection, appropriate systemic bactericidal antibiotic therapy with combined streptomycin-tetracycline, with kanamycin or ampicillin, or with one of the cephalosporins or colistin or polymyxin should be given. In purulent pericarditis the incidence of cure today with appropriate parenteral and local bactericidal antibiotic therapy together with pericardiostomy should approach 90%.

Tuberculous pericarditis. Clinical tuberculous pericarditis is uncommon and is frequently associated with tuberculosis elsewhere in the body. Occasionally it is the predominant part of the clinical picture; rarely it may be the only clinical manifestation of tuberculosis.

The clinical picture of tuberculous pericarditis varies considerably. In about half the cases the diagnosis can be proved by culture. In the other half the diagnosis must rest on clinical grounds, that is, the presence of fever in a young male, usually a Negro, a positive Mantoux reaction, and prompt response to antituberculosis treatment after all other causes of pericarditis have been excluded. All cases of obscure pericarditis should be studied thoroughly microbiologically and a precise etiologic diagnosis should be established even if it is necessary to perform an open biopsy of the pericardium.

Before the era of antibiotic therapy the prognosis in patients with tuberculous pericarditis was grave indeed. The mortality rate often was as high as 90%. Occasionally, tuberculous pericarditis has been known to subside spontaneously. Death from this infection, if untreated, is usually due to dissemination of tuberculosis from some other focus or from the mechanical effects of pericardial involvement. Death may be due to congestive heart failure or to late development of chronic constrictive pericarditis.

With the use of streptomycin alone, initially, a number of observers noted that the mortality from this infection was almost halved. Studies of patients with clinically primary tuberculous pericarditis treated intermittently with streptomycin and para-aminosalicylic acid or isoniazid indicated that the mortality rate in the disease can be as low as 8 to 15%.

The treatment of tuberculous pericarditis today is based on early diagnosis, institution of early antibiotic therapy with combined drugs, adequate rest, aspiration of pericardial fluid for relief of symptoms of cardiac tamponade if necessary, and pericardiostomy if the course of the disease is not satisfactory with antibiotic therapy alone. Since the prognosis has been poor in this type of infection, therapy should be given for a long period, as in tuberculous meningitis; it may be given for as long as one or two years.

Two of the 3 standard chemotherapeutic antituberculosis drugs, with isoniazid as one of the combination, may be used for therapy. Streptomycin, 1 gm., should be given daily for three months and then twice per week for the remainder of the period of therapy. Isoniazid, 300 mg. a day, and sodium para-aminosalicylic acid, 6 gm. per day, should be given orally; when these 2 drugs are used in combination, they may

be given as 1 dose daily in the morning after breakfast. If the response to antibiotic therapy is not good, surgical treatment is resorted to while the patient is maintained on chemotherapy. The factors to consider in evaluating the course of the disease are duration of fever, duration of effusion, progress according to the electrocardiogram, and evolution of the degree of congestion. The last factor may be the most important.

The criteria of inactivity or cure are absence of fever, a normal sedimentation rate, no evidence of congestion, a normal-sized heart with normal pulsations, and a stable though not normal electrocardiogram.

Early diagnosis and early therapy, in the first two or three weeks of the disease, give the best results with antibiotics. If there is any doubt about the diagnosis of tuberculous pericarditis, treatment should be started at once while the results of culture and guinea pig inoculation are being awaited. Nothing is lost by starting treatment early, even if tuberculosis is eventually excluded as the diagnosis. However, much valuable time is lost if one waits four to eight weeks to establish a positive diagnosis.

Acute benign and viral pericarditis. Acute benign or nonspecific pericarditis is not uncommon. The cause remains unknown. No bacteria have been isolated from the pericardial fluid in this type of infection. It usually follows an upper respiratory infection and has been noted after "atypical" or viral pneumonia and in infectious mononucleosis. Some cases are definitely viral in origin. Unequivocal proof of viral etiology is limited to the Coxsackie group of viruses, which have been isolated from the pericardial fluid. With respect to the other viruses the evidence is not as clear-cut, is indirect, and is less convincing, but increasing case reports indicate that other viruses may cause acute benign or nonspecific pericarditis as evidenced by isolation of viruses from the pericardial fluid, throat, stools, or pleural fluid or from more than one of these sources and also by positive results from serologic studies.

All patients suspected of having acute benign pericarditis should be studied for viral infection. Serum obtained during acute and convalescent stages should be tested appropriately. Swabs of the throat and rectum and specimens of pericardial and pleural fluid, if available, should be examined for viruses. Only in this way can the entity of acute benign or nonspecific and viral pericarditis be elucidated and resolved.

Currently there is much interest in perfecting techniques for early viral diagnosis and for investigation of viral chemotherapeutic agents. A number of antiviral drugs are becoming available for study and clinical evaluation, such as 1-adamantanamine hydrochloride (amantadine), which is being investigated for the prophylaxis and treatment of influenza.

In most instances, viral pericarditis is benign and self-limiting and there is little need for specific treatment. Until early diagnosis is feasible and appropriate specific antiviral chemotherapy becomes available, the more seriously ill patients may be given steroids to tide them over. However, before giving steroids, a bacterial cause of the pericarditis should be excluded. One must be sure that tuberculous pericarditis is not present. Fairly prompt clinical improvement, within twenty-four-hours, occurs after steroid therapy is started.

TREATMENT AND PROPHYLAXIS OF STREPTOCOCCAL INFECTIONS AND RHEUMATIC FEVER

Rheumatic fever is definitely related to streptococcal infections and may occur after an infection with any type of group A hemolytic streptococci. A period of several days to several weeks intervenes between the streptococcal infection and the onset of rheumatic fever, with the attack rate being about 3%; the incidence of rheumatic fever, however, is greater in patients who have had previous attacks. Most patients with a classic attack usually develop rheumatic heart disease. Another 3% of patients, following streptococcal infections, develop vague illness with mild symptoms or isolated physical or laboratory signs indicative of rheumatic fever without a definitive diagnosis being made. From the latter group arise the patients with rheumatic heart disease who do not give a history of rheumatic fever.

In patients with streptococcal infections who are not treated with penicillin, the streptococci are not eliminated from the respiratory tract for periods varying from three or four weeks up to four months. It has been demonstrated that rheumatic fever does not occur unless streptococci continue to reside in the respiratory tract. The available data suggest that the development of rheumatic fever requires the presence of living streptococci in the throat, only a few being needed for this purpose.

Rheumatic fever can be prevented if penicillin therapy for streptococcal pharyngitis is given during the latent period of ten to fourteen days after the onset of sore throat; treatment, however, should be given even if a longer period has elapsed without therapy. Thus, any treatment that fails to eradicate the streptococci from the throat does not alter the attack rate of rheumatic fever. Sulfadiazine, a bacteriostatic drug, is completely ineffective in streptococcal infections be-

cause it serves only to suppress rather than kill them.

The treatment for rheumatic fever consists of (1) antibiotic therapy to eradicate streptococci from the throat, (2) antibiotic prophylaxis against future streptococcal infection, (3) restriction of activity and extra rest, and (4) suppression of the inflammatory reaction by the use of salicylates and adrenal steroids.

I shall confine my remarks to the first 2 points. Once the diagnosis of rheumatic fever has been made, penicillin should be given. One intramuscular injection of 1,200,000 units of the long-acting, repository type of penicillin G or benzathine penicillin (Bicillin®) probably represents the best means of eradicating streptococci from the throat. If oral penicillin therapy is given (250,000 units of penicillin V 4 times a day), it should be continued for ten days. For prophylaxis, penicillin should be given at monthly intervals throughout the year. In the young patient, such prophylaxis should be continued for a long time—well into adulthood. After an attack of rheumatic fever in an adult, penicillin prophylaxis should be continued for at least five years and perhaps longer, at least until age 50. Lifetime prophylaxis would be the ideal goal in these patients, but would probably be difficult to achieve.

One may use the sulfonamides or oral penicillin for prophylaxis, and many do, but the results are not as good as with monthly parenteral therapy with Bicillin®. Inasmuch as the sulfonamides are bacteriostatic rather than bactericidal, their action is suppressive. They do not eradicate the streptococcal carrier state. They can be useful only in preventing new streptococcal infection after the streptococci have been eliminated by penicillin or other antibiotic therapy. Other disadvantages are the risk of serious toxicity, the development of resistant streptococci, and the frequent breaks in the routine. The sulfonamide drugs, given 1 gm. per day, are now considered the second choice after Bicillin®.

Penicillin is the antibiotic of choice in the treatment and prophylaxis of group A hemolytic streptococcal infections. Oral penicillin V in a dose of 250,000 units once or twice a day can be used for prophylaxis and seems to be effective but is considered the third regimen choice. The disadvantages of oral penicillin are the frequent breaks in routine, the irregular absorption of the drug, the cost, and the fact that the minimal effective dose has not been established.

The administration of a single monthly injection of 1,200,000 units of Bicillin® for continuous prophylaxis has much to recommend it; it is reliable, safe, and economical and provides a close patient contact. A single dose eliminates the carrier state, and a break in prophylaxis is less likely to occur. Serious toxicity is rare and no resistant streptococci are produced. The only disadvantages are the moderate local soreness at the site of injection in 5 to 10% of the patients, which is somewhat more than with the injection of procaine penicillin and the fact that injection is required. Recent study indicates that the best prophylactic regimen is the monthly intramuscular injection of Bicillin®. It can be tolerated this way by 90 to 95% of patients.

ANTIBIOTIC PROPHYLAXIS OF BACTERIAL ENDOCARDITIS

Twenty-five to 30% of patients with bacterial endocarditis still die from their infection or complications of their disease despite the progress of antibiotic therapy during the past two decades. Probably the chief reasons for this are late diagnosis of bacterial endocarditis, late adequate therapy, and failure to employ bactericidal antibiotic regimens. A contributing factor to this mortality is the failure in many instances to utilize adequate antibiotic prophylaxis in patients with heart murmurs and heart disease who undergo instrumental diagnostic procedures; minor or major operations, particularly cardiovascular bypass operations; and dental extractions.

The prophylaxis of bacterial endocarditis has been stressed in the recent literature and consists of (1) adequate antibiotic treatment and prevention of streptococcal infection and rheumatic fever, the precursors of rheumatic heart disease, (2) eradication of focuses of infection in patients with valvular heart disease, and (3) appropriate preoperative and postoperative antibiotic therapy in persons with heart murmurs.

The problem of appropriate antibiotic treatment and prevention of streptococcal infections and rheumatic fever has already been discussed. In patients with heart murmurs, focuses of infection should be eradicated. Periapical dental infection should be removed under adequate antibiotic protection. Chronic infection of the sinuses, ears, mastoids, and throat and in the prostate, genitourinary tract, bones, or gastrointestinal tract should be eradicated similarly.

In 1 series of 111 patients with subacute bacterial endocarditis, the underlying heart disease of 100 was rheumatic in origin. Sixty percent of the 100 patients were unaware of the presence of heart disease. These observations stress the need for cardiac examination of all patients undergoing dental extraction or surgical procedures.

A wide variety of conditions may injure

mucous membranes and facilitate the entrance of bacteria into the bloodstream and lead to endocarditis in the presence of valvular damage. The list includes (1) infections, operations, and instrumental diagnostic procedures on the ears, nose, and throat, (2) manipulations and extractions of teeth, (3) endoscopic procedures, (4) infections, instrumental diagnostic procedures, and operations on the genitourinary tract, (5) infections of the skin, pelvis, bones, and gastrointestinal tract, (6) the pneumonias and exanthems, and (7) other conditions such as upper respiratory infections, prostatic massages, enteritis, infections about the toes, delivery in normal pregnancy, and abortions.

It has been estimated that some 25 to 50% of cases of bacterial endocarditis have their origin in dental manipulations or extractions. Patients who are to have dental work should be questioned and examined regarding the presence of a heart murmur or heart disease. Dental extractions should be carried out under adequate antibiotic protection.

The recent literature on antibiotic prophylaxis indicates that there are as many different programs as the number of institutions or men using them. However, experience of the past two decades shows that penicillin G or V in a daily dose of 2 million units given orally or intramuscularly in divided doses before, during, and following diagnostic or surgical manipulative procedures is adequate in most instances. The last dose should be given one-half to one hour before the manipulative procedure. However, cases have been recorded of failure of 2 million units of penicillin G per day in divided doses given every six hours for two days before and for two days after extractions. In 1 patient a penicillin-resistant strain of S. viridans was isolated which required 2 units per millimeter of penicillin to inhibit it. Some patients receiving monthly injections of 1,200,000 units of Bicillin® for prophylaxis of rheumatic fever have developed bacterial endocarditis and the organisms recovered were penicillin-sensitive "viridans" streptococci. These patients were successfully treated with larger doses of penicillin G. Monthly intramuscular injection of Bicillin® for prophylaxis of rheumatic fever does not constitute adequate prophylaxis for bacterial endocarditis in patients with heart murmurs.

In vitro and clinical studies indicate that the bactericidal action of penicillin G is enhanced when used together with streptomycin against most strains of nonhemolytic streptococci. This has been demonstrated clinically in the treatment of both the "viridans" and the enterococcal forms of streptococcal endocarditis. Studies have also indicated that combined penicillin-streptomycin has greater effect in reducing the bacterial flora of the mouth than has penicillin alone.

It would seem from these in vitro and clinical studies that the combination of procaine penicillin G and streptomycin in divided doses given intramuscularly for twenty-four hours before and twenty-four hours after the contemplated procedure would be the best prophylaxis in patients with heart murmurs who need instrumental diagnostic procedures or dental operations. We have found it satisfactory to use 1 million units of aqueous procaine penicillin G and 1 gm. of streptomycin every twelve hours intramuscularly and one hour before the operation and then every twelve hours after operation for 2 doses. Smaller doses of streptomycin are given if renal function is not adequate.

In patients who are sensitive to penicillin, erythromycin may be used for prophylaxis; 0.5 gm. is given orally every six hours the day before, the day of, and the day after the surgical procedure, with an intramuscular injection of 200 mg. being given one-half to one hour before extractions. Inasmuch as cephalosporin C derivatives such as cephalothin or cephaloridine are bactericidal and not cross-allergenic with penicillin G, they may prove to be satisfactory substitutes for parenteral administration for prophylaxis in these patients. Inasmuch as the penicillin G and streptomycin combination is bactericidal and gives enhanced antibacterial effect against streptococci and since these are the drugs of choice in the treatment of streptococcal endocarditis that arises from dental procedures, it seems good policy to use them in prophylaxis also.

In enterococcal endocarditis a significant number of patients do not give a previous history of heart disease, heart murmur, or rheumatic fever. It is probable that in these patients the infection occurs on normal valves. Support for this thesis was obtained by review of necropsy cases of enterococcal endocarditis in which a definite statement was made regarding the presence or absence of underlying heart disease; this showed that the incidence may be as high as 60%. This figure is at variance with the currently accepted opinion that bacterial endocarditis rarely affects the normal heart valve.

About half the enterococcal valvular infections result from transurethral operations or instrumentation. In about half of these in turn, the patient has no history of heart disease or heart murmur. Since patients with or without heart murmurs are likely to develop enterococcal endo-

carditis following urologic operations or instrumental manipulation, antibiotic prophylaxis assumes an important place in their management. It would seem that the combination of penicillin G and streptomycin as outlined above would be best also for antibiotic prophylaxis in these patients. We have employed this regimen, continuing the prophylaxis postoperatively until one day after the urethral catheter is removed in patients with a heart murmur and in patients without a heart murmur who have had pus or bacteria on urine culture. We have not seen enterococcal or other forms of bacterial endocarditis develop when this program was carried out preoperatively in patients with or without heart murmur.

The ideal antibiotic for the prophylaxis and treatment of bacterial endocarditis has not yet appeared. Possibly, further biochemical and pharmacological research will lead to the discovery of improved broad-spectrum bactericidal antibiotics that will be more effective against gram-negative and gram-positive microorganisms and can be used safely, with minimal side effects, to ensure adequate protection.

The incidence of bacterial endocarditis has markedly decreased over the past two decades as compared with that of the preantibiotic era. It is hoped that more vigorous early treatment and prophylaxis of patients with beta-hemolytic streptococcal disease and patients with heart murmurs will help to lessen the incidence and decrease the mortality of bacterial endocarditis.

URETEROCELE apparently results from weakness in the wall of the terminal ureter and narrowing of the meatus. The congenital deformity is commoner in women than in men. Excretory cystograms usually show a diagnostic cobra-head deformity, with increased density in adults. A constant sign is ureterectasis of the pelvic portion of the associate ureter. In adults, symptoms include flank pain, urinary frequency, urgency, dysuria, fever, hematuria, and urinary retention. Children often are seriously ill, with vesical neck obstruction, abdominal distension, interruption or urinary stream, overflow, incontinence, acute urinary retention, ipsilateral renal or ureteral pain, and fever. When urinary flow is obstructed, operation is required and is usually done transurethrally. Children may need extensive surgery.

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KETOTIC HYPOGLYCEMIA is effectively treated by diet. This form of carbohydrate derangement, possibly the most common hypoglycemic condition in childhood, rarely occurs before 18 months of age. The periodicity of the illness and the ease with which it can be controlled probably obscure its recognition and diagnosis. A ketogenic diet precipitates symptoms of central nervous system dysfunction in susceptible children but provokes only hypoglycemia and ketonuria in healthy children. Induction time after carbohydrate deprivation suggests failure of homeostasis after depletion of glycogen stores in the liver. Glucose corrects the ketosis caused by decreased catabolism of fatty acids. Therapy is based on educating parents of the patients to provide adequate caloric intake during the child's waking hours, especially before retiring. Urine should be tested for acetonuria at bedtime, on arising, and particularly during all incidental illnesses. The need for immediate increases in carbohydrate intake for ketonuria must be emphasized.

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Cutaneous Manifestations of Some Internal Diseases

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TIME DOES NOT PERMIT a complete review of the protean signs of systemic disorders; hence, only a few have been selected for discussion in this presentation.

Although there have been many classifications of cutaneous xanthomatosis, the one proposed by McCleary[1] in 1959 seems most acceptable.

CUTANEOUS XANTHOMA

I. Associated with elevated blood cholesterol but normal neutral fat levels:
   A. Primary xanthoma tuberosum
      1. Xanthoma palpebrarum (xanthelasma)
      2. Generalized xanthomatosis of the tendon sheaths
   B. Secondary xanthoma tuberosum
      1. Liver disease
      2. Hypothyroidism

II. Associated with elevated neutral fat levels:
   A. Idiopathic
   B. Secondary
      1. Diabetes
      2. Glomerulonephritis
      3. von Gierke's disease

III. Associated with normal blood lipid values:
   A. Nevoxanthoendothelioma (juvenile xanthogranuloma)
   B. Histiocytosis X
   C. Xanthoma disseminatum

Patients with xanthomas characterized by hypercholesteremia have clear blood serum. There is a cloudy or milky serum only when the neutral fat is elevated. The cutaneous lesions of individuals who have idiopathic hypercholesteremia are practically identical with those who have hyperneutrolipemia. About 60% of the patients with xanthelasmas of the eyelids do not have hyperlipemia. They probably represent an abortive form of xanthoma tuberosum.

In group III, characterized by normal blood lipids, several disorders are included which are characterized by xanthomatous eruptions, but which do not have an actual disturbance of lipid metabolism.

CLINICAL PICTURE

1. Xanthoma palpebrarum (xanthelasma). In this type yellow plaques and papules are limited to the eyelids. In my opinion excision is the best form of treatment. A local anesthetic such as a 1% solution of lidocaine hydrochloride (Xylocaine®) is injected into the loose tissues beneath so that the plaque is raised above the surface of the surrounding normal skin. The lesion can then be removed easily with small, curved eye scissors. Suturing is rarely necessary and bleeding, which as a rule is slight, can be controlled by pressure. Chemocautery, such as trichloracetic acid, has also been used as well as electrodestruction by desiccation or cauterization, but healing is slower and thick scars are more apt to occur.

2. Eruptive type. The disorder is characterized by a widespread or generalized eruption consisting of small yellowish-orange papules or nodules which usually occur suddenly and have no predilection for any specific area. Xanthoma diabeticorum is a good example. The lesions may also appear in patients with hypothyroidism or disease of the liver.

3. Xanthoma tuberosum. The lesions are nodules or plaques and are usually located on the knees, elbows, eyelids, ankles, knuckles, and buttocks. Tendon sheaths may be involved occasionally with or without cutaneous lesions, and there may be hypercholesteremia or hyperneutrolipemia. The cutaneous lesions show little tendency to regress. The life expectancy is shortened by hypertension, cardiovascular accidents, and hepatic complications.

4. Mixed type. Occasionally in liver disease

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the original lesion may be of the eruptive type but tuberous nodules may develop later over the extensor surfaces of the extremities such as one sees in ordinary xanthoma tuberosum.

5. Xanthoma disseminatum. This is an exceedingly rare type of xanthoma and the lesions are small orange or yellow papules located in the axillas, groins, flexor surfaces of the extremities, and mucous membranes. These locations stand in direct contrast to ordinary xanthoma tuberosum in which the lesions are on the extensor surfaces. Blood lipids are normal in this group.

6. Histiocytosis X. This category includes eosinophilic granuloma of bone, Schüller-Christian disease, and Letterer-Siwe disease, all of which are basic disorders of the reticuloendothelial system rather than primary disturbances of lipid metabolism.

The mildest form is eosinophilic granuloma of bone which is characterized usually by a single lesion occurring in children or young adults.

Letterer-Siwe disease manifests itself in infancy or early childhood. It is usually fatal and the lesions are widely distributed through the soft tissues, especially adipose, and the skeleton. There may be enlargement of the spleen, varying degrees of hepatomegaly, and osseous involvement. Purpura is usually a prominent feature. The cutaneous eruption may occur on the scalp, neck, face, trunk, and extremities, and most lesions are hemorrhagic. The lesions on the scalp may simulate seborrheic dermatitis.

Schüller-Christian disease, as a rule, is more chronic but may be rapid and fatal. The characteristic triad of symptoms includes exophthalmos, diabetes insipidus, and osseous lesions. Brown pigmentation and nodular xanthomas have also been reported to be associated with the disorder.

Therapy. There is no satisfactory treatment for xanthoma tuberosum. A low-fat, low-calorie diet may result in a decrease of blood cholesterol and of the size of the nodules but not in complete recovery. I have had little experience with drugs such as aluminum nicotinate which are supposed to reduce the amount of cholesterol in the serum and tissues. Surgical excision may be employed for large xanthomas and lesions on the tendon sheaths. Lever,[2] in 1954, found that the intravenous injection of 50 mg. of heparin diminished the amount of cholesterol in the plasma in primary hypercholesteremic xanthomatosis and the amounts of all of the lipids in idiopathic hyperlipemia. He believed that prolonged therapy with heparin might reduce the elevated lipid levels in both diseases.

NECROBIOSIS LIPOIDICA

This disorder is characterized by plaques which are usually asymptomatic and located on the lower extremities, especially around the ankles.

It occurs usually, but not exclusively, in patients with diabetes mellitus. In some individuals without definite diabetes there is a family history of the disease or there are abnormalities in glucose tolerance.

The individual plaques are oval with well-defined borders and a smooth waxy surface. The central portions may be somewhat sunken and atrophic, and dilated vessels usually are present on the surface. The centers of the lesions are usually yellow or orange while the peripheries are violet. The surrouding skin is normal. The onset is insidious and there are no symptoms unless ulceration occurs.

Treatment is unsatisfactory. Excision and subsequent skin grafting have cured an occasional patient. A few individuals seem to have benefited by sublesional injections of steroids. As in all patients with diabetes or arteriosclerosis of the lower extremities, the careful avoidance of trauma is important. Special attention should be paid to keeping the feet and lower extremities clean and dry. Diabetes, if present, should be carefully controlled even though this usually does not result in disappearance of the lesions.

PSEUDOXANTHOMA ELASTICUM

This disorder represents the mucocutaneous expression of a widespread hereditary degenerative process in the elastic tissues which is usually also represented by angioid streaks of the retina and circulatory disturbances. The disease is rare and no racial predilection has been noted. It occurs slightly more frequently in males than females and usually arises insidiously in childhood or early adult life.

Cutaneous changes. The lesions are asymptomatic, 1 to 2 mm. in diameter, and either white or light yellow. They are firm, discrete, and waxy. As the disease develops, the papules become confluent to form smooth yellow plaques which may be as large as the palm and elevated 2 to 5 mm. above the surrounding skin. The skin may become wrinkled and loose and hang in folds from its underlying attachments, frequently resembling that of a plucked chicken. The areas most frequently involved are the sides of the neck, axillas, groins, cubitals, popliteals, and the upper inner surfaces of the thighs. Rarely the entire body surface may be affected except the scalp, palms, and soles. The oral mucosa is involved occasionally, especially the inner surface of the lower lip.

Angioid streaks in the eyes have been found in 50 to 90% of the patients. They are usually bilateral and are thought to be due to rupture of the elastic tissue.

The third group of symptoms is associated with degeneration of the elastic tissue in the arteries and occasionally secondary deposition of calcium. This leads to hypertension, cardiac enlargement, coronary insufficiency, and decompensation. There may be dilation or aneurysm of the aorta. Degeneration of the elastic tissue in other organs may lead to psychosis, epilepsy, or hemorrhages from the nose, stomach, intestines, bladder, and uterus.

The outlook is poor. The cutaneous changes are of little importance other than cosmetic, but involvement of the arteries may lead to early death.

Unfortunately there is no satisfactory treatment for the correction of the underlying elastic tissue degeneration. Plastic surgery may be employed to correct the hanging folds at the sides of the neck or elsewhere.

PORPHYRIA

Porphyria refers to a group of inborn errors or porphyrin metabolism manifested clinically by cutaneous photosensitivity and abdominal and neurological disorders. Ratner and Dobson,[3] in 1964, suspected that an aberration in purine metabolism may represent part of the defect in some cases of porphyria. The epidemic of hepatic cutaneous porphyria in Turkey, caused by the ingestion of hexachlorbenzene, suggests that the disease may be totally acquired without an underlying hereditary metabolic defect.[4,5] Bleiberg and colleagues,[6] in 1964, reported porphyria cutanea tarda in 29 patients working in a chemical factory engaged in the manufacturing of 2, 4-dichlorphenol and 2, 4, 5-trichlorphenol substances which are used as weed killers and are apparently hepatotoxic.

A classification of the various types of porphyria follows:

1. Erythropoietic porphyria:
   - A. Congenital photosensitive porphyria (Günther)
   - B. Erythropoietic protoporphyria
2. Hepatic porphyria. In this type the liver is the principal or only site of abnormal porphyrin formation:
   - A. Intermittent or acute type—abdominal or nervous manifestations
   - B. Porphyria cutanea tarda—with photosensitivity without other manifestations
   - C. Mixed type—photosensitivity with intermittent abdominal or nervous manifestations
   - D. Latent type—asymptomatic variations of porphyrin metabolism among relatives of those with manifest disease.

Erythropoietic porphyria. This is extremely rare and constitutes less than 1% of the patients with porphyria. It is characterized by onset in early life, even shortly after birth. The urine is red and there is photosensitivity, with the formation of bullae on the exposed parts, especially the knees, ears, and hands. There may be linear scars around the mouth which give the face a puckered look. The skin may be hyperpigmented, and moderate hypertrichosis of the face and extremities is common. The teeth are brown or brownish-red and fluoresce when exposed to ultraviolet light.

In this form of the disease the bone marrow contains large amounts of porphyrin. This has been shown to be a mixture of uro-, copro-, and protoporphyrin. Circulating erythrocytes also contain excessive amounts of uro- and coproporphyrin, and the spleen is rich in these substances.

Erythropoietic protoporphyria. This form of porphyria was discussed in 1964 by Redeker and Bronow.[7] They studied 3 patients with erythropoietic protoporphyria who were the first to be reported in this country. There was marked elevation of protoporphyrin in the free erythrocytes and feces similar to the cases reported from Europe. The photocutaneous eruption, observed in all 3 patients, was considered to result from excessive protoporphyrin in the plasma. The authors stated cutaneous features were those of hydroa aestivale and these observers proposed that hydroa aestivale is a form of erythropoietic protoporphyria. Their descriptions, however, suggested that the patients had solar dermatitis of the polymorphic type rather than true hydroa aestivale since edema, erythema, and eczemitization were the principal morphological features. The European cases were characterized by recurrent episodes of urticaria following exposure to sunlight. In contrast to erythropoietic protoporphyria, the level of uroporphyrin rather than protoporphyrin is elevated in porphyria cutanea tarda.

Porphyria cutanea tarda. This disorder is of special interest because it is more common, constituting 30 to 40% of cases of cutaneous porphyria. It usually occurs between the ages of 30 and 60, although occasional cases have been noted in childhood. Males are affected more frequently than females.

The cardinal features are: (1) bullae, (2)

hyper- and hypopigmentation, (3) hypertrichosis, and (4) eczematous or sclerodermoid plaques. Vesicles and bullae as large as 2.5 cm. in diameter develop on the exposed parts, usually the face, neck, and hands following exposure to sunlight or other types of trauma. They occasionally become infected and crusted and may form deep ulcers. Healing is slow, with the formation of pigmented or depigmented, irregular, shallow scars. The exposed parts of the skin may be violet or brown in color. Hypopigmentation may be diffuse or mottled and sometimes resembles vitiligo. Hypertrichosis occurs especially on the face and back. Yellow sclerodermoid plaques have been observed on the face, neck, back, or extremities of some of the patients. The urine may be dark and fluoresces red when exposed to filtered ultraviolet radiation.

Some patients who have porphyria cutanea tarda are chronic users of alcohol or barbiturates. Other drugs, including chloroquine and antimalarials, have been incriminated in some cases. The life expectancy in porphyria cutanea tarda depends on the extent of progression of the associated liver disease. Biopsy of the liver or examination of the organ at necropsy may show varying degrees of fatty degeneration or cirrhosis. The organ contains large amounts of uroporphyrin. In the hepatic forms of porphyria the amount of porphyrin in the bone marrow is normal.

Treatment consists of a regimen to improve hepatic dysfunction and complications of liver disease. Alcohol and barbiturates should be avoided. The cutaneous lesions are benefited by avoidance of exposure to sunlight and trauma. Occasionally corticosteroids have produced improvement and in certain cases a short course is indicated. If there is no benefit within a few days they should be discontinued.

Lecture given at the Center for Continuation Study in a Course in Dermatology, October 10-12, 1963.

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AUSCULTATORY blood pressure is consistently increased in hyper- and normotensive subjects by downward displacement of the arm and, largely, by the hydrostatic factor. The supine position is recommended or standard positioning of the forearm at the phlebostatic axis, the level of the junction of the fourth intercostal space with the lateral border of the sternum. Blood pressure was recorded in 139 middle-aged men while they sat for five minutes, the right arm pronated in a supporting trough fixed at a 30° angle from the sagittal plane of the trunk. Elbows were positioned at the level of (1) the sternomanubrial junction, (2) the fourth intercostal space at the sternum, and (3) the xiphosternal junction. The mean difference between the second and first positions was 5 mm. Hg systolic and 4.6 mm. diastolic and between the third and second positions, 6 mm. Hg systolic and 5.7 mm. diastolic.

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Gummatous Tracheobronchial Ulcers with Fatal Hemorrhage

Report of a Case

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TODAY it is quite unusual to encounter gummas in this part of the world, and more so gummas of the bronchi and trachea. Spencer[1] stated in his recent publication that "An uncommon form of syphilitic lesion, example of which may still be found in the older museum collections, is the gummatous ulcer of the main bronchi and trachea . . . ." Even in the earlier years, when syphilis was not too uncommon, gummatous changes of the trachea and bronchi were still rare. Symmers,[2] in 1916, reviewed 4,880 autopsies and found 314 cases with acquired syphilis, and 33 of the latter showed involvement of the respiratory tract. Lesions in the trachea were present in 4 instances with ulcerations or fibrosis.

This is to report a recently observed case of gummatous tracheobronchial ulcers with a massive fatal hemorrhage.

CASE REPORT

A 70-year-old male, while driving a small truck on his way to see a physician for a nosebleed, hit a parked truck. Little damage was noted to either truck but he was found unresponsive with blood over his face. He was taken to a nearby hospital and pronounced dead on arrival. Since external injuries were not seen, a county coroner ordered an autopsy to determine the actual cause of death, which was presumed to have occurred prior to the accident.

Gross pathology. Externally only a small abrasion of the facial skin was noted. Both nostrils were filled with a moderate amount of clotted blood and the oral cavity contained 10 ml. of blood. No other abnormalities were seen in the oral cavity. The heart weighed 660 gm. and showed moderate hypertrophy of the left ventricle with the thickness of 19 mm. The aortic cusps were slightly calcified but free of deformities. The ascending aorta was considerably dilated, and the intimal surface had a tree-bark appearance with patchy atheromatous changes. Both lungs weighed 1,000 gm. together; they showed smooth pleural surfaces, and both apices were thickened. The pulmonary parenchyma was moderately emphysematous, but no bronchiectasis or granulomatous foci were found. The trachea and bronchi were filled with partially clotted blood. The bifurcation of the trachea and the right bronchus showed 2 longitudinal ulcers. One ulcer was present at the bifurcation extending to the upper portions of both right and left bronchi, and measured 4 cm. in length and 2 cm. in width (Fig. 1). The other was seen in the right main and lower lobe bronchi and measured 3 × 1 cm. (Fig. 2). The border of the ulcers was irregular with minimal underminings. Several bronchial cartilages were eroded and the sharp edges of the broken cartilages protruded into the ulcers. The bottom of the ulcers was firm, uneven, yellowish-white, and covered with fibrin and clotted blood. The peritracheal and peribronchial tissue surrounding the ulcers formed a firm, pale yellow mass, measuring a few centimeters in depth. Several lymph nodes along the right bronchus and around the bifurcation were similarly replaced by pale yellow tissue, though rubbery in consistency, and some of them were adherent to the peritracheal and peribronchial mass. On the average those enlarged lymph nodes measured 2.5 cm. in diameter.

The liver weighed 2,100 gm. and showed marked shrinkage of the left lobe, with massive

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Fig. 1. An ulcer at bifurcation of trachea extending to left main bronchus; arrow indicates undermined irregular border. An enlarged lymph node and part of peribronchial mass are also seen.

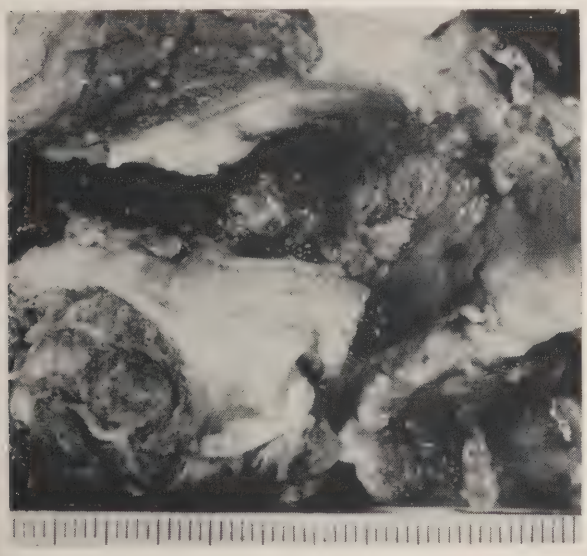


Fig. 2. An ulcer in right bronchus covered with small amount of fibrin and blood. The base of ulcer is very uneven. A moderate thickening of peribronchial tissue is again noted. The mucosa surrounding ulcer shows irregular thickening.

adhesions to the diaphragm. Almost entire left lobe of the liver was replaced by numerous conglomerate yellowish-white nodules, 1 to 3 cm. in diameter. Such nodules were also seen in the median portions of the right lobe. Some nodules revealed central necrosis, and the tissue between the nodules was markedly fibrotic. The adhesions between the diaphragm and the liver were due to a similar granulomatous process, and the thickness measured up to several centimeters. The remaining right lobe disclosed a nutmeg appearance but was not cirrhotic.

The epipancreatic lymph nodes were enlarged with yellowish-white tissue, rubbery in consistency and partly necrotic, while no abnormalities were noted in the pancreas.

Both testes showed slight atrophy. The brain weighed 1,260 gm. and revealed atrophy of the parietal lobes, but no thickening of the meninges was present.

Histopathology. Hematoxylin and eosin stains: The sections of the trachea and bronchi showed the necrotic mucosa with the formation of ulcers (Fig. 3). The base of the ulcers had reached to or undermined the cartilages, and there was evidence of recent hemorrhage and active inflammation. Deeper in the peritracheal and peribronchial mass, a granulomatous process with central necrosis was under way. The necrosis was of coagulation type and some of the original structures could still be recognized in a faint shadowy appearance. Directly surrounding the necrosis was a zone of lymphocytes and plasma cells. The second zone, characterized by epithelioid cells, histiocytes and a few giant cells, and the outermost third zone of fibrosis encircled the inner zone of round cells. Many small arteries within the zone of fibrosis showed a marked thickening of the intima (Fig. 4). The periarteritic changes were less evident. The pulmonary parenchyma showed only the emphysematous changes, but no evidence of the syphilitic involvement, either in the fibrotic or gummatous form, was seen.

The similar granulomatous process with coagulation necrosis was noted in sections taken



Fig. 3. A section taken from edge of ulcer, including a part of cartilage. (A) Coagulation necrosis, (B) lymphocytic and plasmocytic infiltration, (C) fibrosis, and (D) acute inflammation. (Hematoxylin and eosin, × 6).

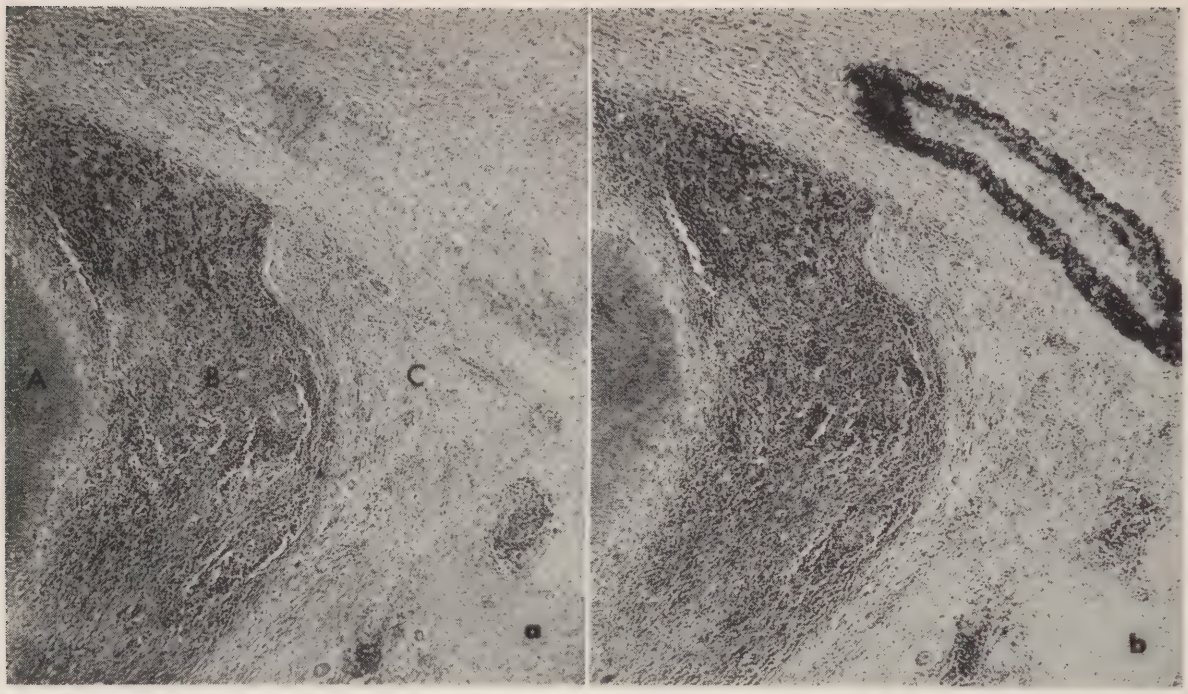


Fig. 4. Sections taken from border of coagulation necrosis. Section b shows small artery embedded in zone of fibrosis. (A) Coagulation necrosis, (B) lymphocytic and plasmocytic infiltration, and (C) fibrosis. (a: hematoxylin and eosin stain and b: Verhoeff-van Gieson stain, × 30).

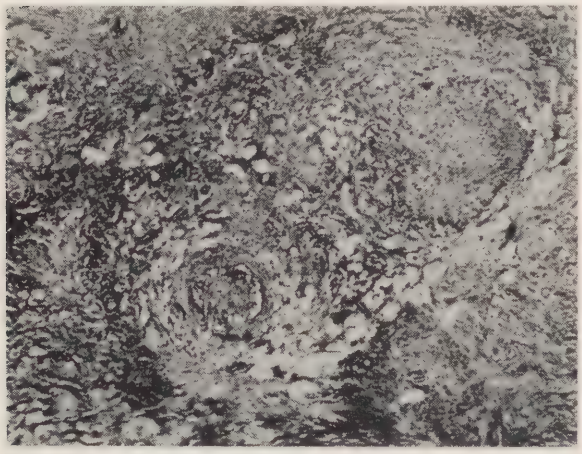


Fig. 5. A section taken from coagulation necrosis, showing preservation of elastic fibers and collagen bundles, though both are fragmented. (Verhoeff-van Gieson stain, × 200).

from the left lobe of the liver. The remaining hepatic tissue between the nodules was cirrhotic and the portal canals showed a collection of lymphocytes and plasma cells. Most of the right lobe of the liver revealed central atrophy of the lobules and a heavy lymphocytic infiltration in the portal canals.

The peribronchial and epipancreatic lymph nodes showed similar granulomatous inflammation as seen in the bronchus and liver.

The sections taken from the ascending aorta revealed disrupted elastic laminae and the infiltration of lymphocytes and plasma cells around vasa vasorum.

Stains for the connective tissue. The Verhoeff-van Gieson stain showed fairly well preserved elastic fibers and some collagen bundles within the central coagulation necrosis and the outer zone of fibrosis (Figs. 4 and 5).

Stains for spirochetes. Both the Levaditi and Warthin-Starry methods did not reveal any spirochetes.

DISCUSSION

Syphilitic lesions in the trachea and bronchi are nearly confined to the tertiary stage, and the involvement with secondary syphilis is extremely uncommon and fleeting in character. It is of little if any clinical significance.

At the beginning of the twentieth century, Conner[3] reviewed 128 cases of the tracheobronchial syphilis found in the literature of the preceding six decades. The trachea alone was affected in 56% of the cases, both the trachea and bronchi in 33%, and the bronchi alone in 11%. The most frequent site was at, or just above, the bifurcation. The lesions could be divided into 4 groups: (1) ulcerations, (2) mucosal fibrosis (scar formation), (3) obliterative endotracheitis or endobronchitis due to gummas, and (4) fibrous peritracheitis. The ulcerations were the most frequent and seen in 44% of cases. More

than one-third of the cases showed only single ulcers. Conner recorded 5 cases of the tracheobronchial hemorrhage due to the gummatous erosions into the aorta, pulmonary artery, vena cava, and bronchial artery. Four patients died.

Other complications of the tracheobronchial gummas were suffocation due to the stenosis of the lumen[3,4] which may suddenly follow the antiluetic therapy.[5] The perforation of the esophagus[6] and the development of purulent mediastinitis[7] have also been reported.

The lesions in the trachea and main bronchi can easily be reached by the use of bronchoscope, but the establishment of the specific tissue diagnosis for syphilis from the biopsy specimen is often difficult.[8] In some instances the definite diagnosis depended entirely upon the clinical response to the antiluetic therapy.[9,10]

The association of tracheal and bronchial syphilis with the luetic lesions elsewhere in the respiratory tract was fairly frequent.[3] Thirty percent of the cases were associated with laryngeal lesions; 20% had luetic changes in the palate, nose, or mouth; and 18% showed pulmonary involvement, either in interstitial or gummatous form.

On the other hand, the combination of hepatic and bronchial syphilis is quite rare. Symmers and Spain[11] reviewed 4,880 autopsies and found 35 cases of hepatic gummas. Only 1 case showed the combination with the syphilitic tracheitis. Bucher and Ono,[6] Herzog and Conrad,[5] and Howard[12] have reported similar findings.

SUMMARY

A 70-year-old male died of a sudden massive hemorrhage from the gummatous ulcers of the trachea and bronchi. The concomitant gummatous lesions were found in the liver and lymph nodes at autopsy.

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POSTPARTUM PITUITARY NECROSIS is a common cause of pituitary insufficiency in women during reproductive years and affects gonadal, thyroidal, and adrenocortical functions. Both posterior and anterior lobes may be involved, resulting in diabetes insipidus. The necrosis, Sheehan's syndrome, usually results from immediate postpartum hemorrhage or shock; such patients should be observed for at least one year, with supplementary sodium chloride and cortisone during stress periods. Signs and symptoms include pallor, dry skin, scanty or no axillary and pubic hair, vaginal mucosa atrophy, extreme fatigue, amenorrhea, sporadic unconsciousness, hot flashes, anemia, nausea, or anorexia. Lymphocytosis, elevated sedimentation rate, and hypoglycemia are frequent. Urinary excretion of 17-ketosteroids is low or absent, basal metabolic rate is low, and pituitary gonadotrophin often is lacking. About 8% of patients with moderate and 53% with massive hemorrhage have hypopituitarism.

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The History of Radiology in South Dakota

DONALD H. BREIT, M.D.

Sioux Falls

Radiology was introduced into South Dakota in the gas tube era by Nelius J. Nessa, M.D. Dr. Nessa was graduated from the University of Minnesota School of Medicine in 1904. After internship and brief general practice in Brewster, Minn., he moved to Sioux Falls and joined Dr. R. G. Stevens, a general surgeon, in operating Good Samaritan Hospital. He became interested in radiology and took a course from Dr. James Case of Chicago in 1915. He returned to Sioux Falls and, in association with Drs. E. E. Gage and Guy Van Demark, continued his general practice but devoted as much time as possible to X-ray work. He used a gas tube in a lead glass bowl energized by an induction coil. In 1918 he enlisted in the U.S. Army and had further training in radiology at Fort Oglethorpe in Georgia and at Great Lakes Training Station, Chicago.

After his discharge in 1920, he was a member of a group that organized the Sioux Falls Clinic. He limited his practice to diagnostic and therapeutic radiology and became the first specialist in radiology in South Dakota. He was joined in July of that year by W. S. Beckstrom, a well-trained technician who had studied at the Army Medical School and Johns Hopkins Hospital.

The X-ray department in the Sioux Falls Clinic was quite well furnished with the most modern and up-to-date equipment of that time. Two complete Schnook units were installed, a 180-KVP for intermediate and deep therapy and a 135-KVP for diagnostic procedures and superficial therapy. Coolidge tubes in open lead bowls were used overhead for diagnosis and therapy, and a tube beneath the table served for fluoroscopy. An upright fluoroscope was installed, and a curved table with a curved bucky for radiographic work completed the installation.

Dr. Nessa was also radiologist for both Sioux Valley and McKennan hospitals. Films were taken there and in homes by Mr. Beckstrom. He used a Scheidel-Western gas tube unit, suitcase type, with a portable tube stand. Later, a Coolidge Model F portable unit was used. The films were returned to the Sioux Falls Clinic for processing and for interpretation by Dr. Nessa.

St. Luke's Hospital in Aberdeen was opened in 1928, with Dr. Paul V. McCarthy as radiologist. He was the second physician in South Dakota doing radiological work as a specialty. He received his medical degree from St. Louis University and was stimulated in radiology as an intern at St. Louis City Hospital by Dr. L. R. Sante. As a student, he knew Dr. Sante when he was establishing himself in St. Louis as a radiologist after World War I. Dr. McCarthy returned to St. Louis before 1928 and spent some time with Dr. Sante at St. Louis City Hospital.

During the early 30s, times were not too prosperous in South Dakota. Dr. McCarthy found it necessary to do general practice in addition to his X-ray work. Several practitioners in the state who started doing X-ray work during the era have continued, to some extent. The number of nonradiologists doing X-ray work and amounts they are doing have been gradually decreasing.

Dr. McCarthy also used a Schnook apparatus with a motor-driven disk capable of energy up to 135-KVP. This unit was used for diagnostic and therapeutic procedures. For therapy a special tube in a lead bowl was used; for diagnosis an overhead tube with a fluoroscopy tube beneath.

In 1939, shock proof equipment was installed in the hospitals in Sioux Falls and Aberdeen. By that time, radiology was well established as a specialty in eastern South Dakota under the leadership of Drs. Nessa and McCarthy.

Shortly thereafter, the spotlight shifted from the eastern to the western part of the state and to Dr. J. Richard Fuchlow. He became the first radiologist to serve the Black Hills area as a specialist. He established practice in Rapid City in 1941. He had been an X-ray technician who studied medicine, received his medical degree, and specialized in radiology. He retired in 1944 and died of a coronary occlusion.

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Dr. Ernest H. Brock, a Texan, replaced Dr. Fuchlow in 1944 and opened an office in the old Black Hills General Hospital. In 1947 he opened a private office but continued to serve both Rapid City hospitals as well as Veterans Hospital at Fort Meade and St. Joseph's Hospital in Deadwood. In the latter part of 1950, he suffered a coronary occlusion and retired to Texas. Drs. Alton J. Saxton and George F. Wood, Jr., took over his practice. Dr. Saxton was from Lincoln, Nebr., and Dr. Wood from St. Paul, Minn. Both were certified radiologists and continued Dr. Brock's practice and served those hospitals which he had served. In addition, they extended radiological service to Homestake Hospital in Lead, Veterans Hospital in Hot Springs, and the community hospitals of Spearfish and Belle Fourche. They were joined in 1957 by Dr. John Hewitt.

Dr. Hans Jacobi was another pioneer radiologist in eastern South Dakota. He received his medical degree in Germany and was trained in radiology at Breslau. He came to Huron May 1, 1943, and was the first specialist in radiology in that community. He became a member of the staff of the Huron Clinic and Sprague Hospital. St. John's Hospital opened in 1947, and he was the radiologist for that institution. He died in 1958 at the age of 55.

Huron was without permanent radiological service until February 1960, when Dr. G. M. Huet arrived to serve the community and the hospital as a radiologist.

During the latter part of World War II, Dr. Marianne Wallis, a fine foreign-trained radiologist, assisted Dr. Nessa. In 1946, Dr. Donald H. Breit of St. Joseph, Mo., joined Dr. Nessa in Sioux Falls and became the sixth radiologist to engage in specialty practice in South Dakota. He received his medical degree from Baylor University, was trained in surgery, and was in surgical practice before entering the field of radiology. He completed a three-year residency training program at University of Nebraska Hospital under the supervision of Dr. Howard B. Hunt. He spent an extra year assisting Dr. Hunt in his private practice at Nebraska Methodist Hospital and teaching and doing plastic surgery at the University Hospital. Drs. Nessa and Breit remodeled the radiology department of the Sioux Falls Clinic and installed new and modern equipment. They continued serving both Sioux Falls hospitals, McKennan and Sioux Valley, and were consultants for the Veterans Administration Center.

In July 1948 Dr. C. Stanley Larson, a native of Sioux Falls, joined Drs. Nessa and Breit in partnership practice of radiology. Dr. Larson received his radiological training at the Lahey Clinic but came to Sioux Falls from a practice in Corpus Christi, Texas.

Dr. Nessa died in 1948, and the practice was continued by Drs. Breit and Larson. Dr. Donald J. Peik of Minnesota joined the partnership in July 1951 after completing his residency in Milwaukee. Dr. Bryson R. McHardy, also from Minnesota, joined the partnership January 1, 1959, after completing his residency in Chicago.

Modern radiology was brought to Yankton in July 1949 by Dr. James P. Steele. A native of Kentucky, he received his radiological training at Louisville General Hospital, Mallinckrodt Institute of Radiology, St. Louis, and St. Joseph's Mercy Hospital, Ann Arbor, Mich.

Dr. Saul Friefeld settled in the Brookings area in March 1950 and provided the first regular radiological service to Brookings, Madison, Flandreau, Lake Preston, Volga, and Estelline. The medical population declined in Volga and Estelline, and he ceased serving those communities. He later added Marshall and Tyler in Minnesota.

Pierre, the capital city in central South Dakota, was one of the last major cities in the state to be served by a specialist in radiology. Dr. Hubert E. Werthmann located there in 1959. A native of Germany, he received his medical education there but had his training in radiology under Drs. Leo Rigler and H. O. Peterson at the University of Minnesota Hospital as a Mayo Fellow.

Dr. Warren S. Peiper began radiological practice in Mitchell, one of the larger cities in eastern South Dakota, in November 1953. He extended service to Parkston and Chamberlain.

Watertown was the last of the larger communities in South Dakota to have the services of a radiologist as a specialist. Dr. Charles F. Ryan established practice August 1, 1957. He received his training at Albany and came to the state immediately after his radiology residency.

In recent years, several radiologists have come to South Dakota. A few have moved to other locations. The larger communities, as well as most of the smaller ones, have radiological coverage. Although most communities are well covered, more radiologists are needed to lighten the load and further increase coverage. As of 1964, there are 16 radiologists in the state, 15 of whom are certified by the American Board of Radiology. Several teaching programs have been established for training technologists. However, more students apply than can be accommodated.

The progress of radiology in South Dakota, since its rather recent beginning, has been gratifying. Indications are that it will continue to go forward at a rapid pace.

Elias Potter Lyon, M.D.

Scientist, Administrator, Educator, and Humanitarian

A Personal Tribute

J. ARTHUR MYERS, M.D.
Minneapolis



WHEN E. P. LYON attained retirement age in 1936, he had served as medical school dean longer than anyone in the United States. From 1907 to 1913 he was dean of the school of medicine at St. Louis University, and from 1913 to 1936 he was dean at the University of Minnesota.

He was born on a farm near Cambria, Michigan, Oct. 20, 1867. His father was a sawmill boss and while Elias was still in babyhood the family moved to Hillsdale. After graduation from high school Elias went to Chicago where he spent one and one-half years delivering milk. He then felt the need of more education so he returned to Hillsdale and enrolled in the commercial department of Hillsdale College. He had a vacant hour in his course to fill so he took botany. There he became interested in science and went on to the Bachelor of Science degree in 1891. It was then thought that a Bachelor of Arts degree was superior; therefore, he continued and took that degree in 1892. He then procured a job at Harvard School, a preparatory school which was affiliated with the developing University of Chicago. As he taught in this preparatory school, he took postgraduate work at the University of Chicago. In 1894 he served as biologist with Cook's Greenland expedition. He later taught at the Southside Academy in Chicago, but stopped teaching for full-time work at the university where he was awarded his Ph.D. degree in 1897.

That year the Bradley Institute was founded in Peoria, Illinois, and Lyon was chosen to head the department of biology. Three years later, in 1900, the Rush Medical College became affiliated with the University of Chicago and Lyon was called back as first assistant in the department of physiology.

He went to Naples, Italy, in 1902 to work on artificial parthenogenesis. While there, the head of the department of physiology at the University of Chicago took a position at the University of California, and Dr. Lyon was called back from Italy to become acting head. There he knew George E. Vincent, dean of science, literature, and arts. In 1904 he became professor and head of the department of physiology at St. Louis University School of Medicine.

During summer sessions from 1899 to 1910 he was instructor in the Marine Biological Laboratory at Woodshole, Massachusetts. For 3 summers he served as investigator for the United States Fisheries Bureau.

On Jan. 7, 1913, President Vincent, University of Minnesota, explained his plan for reorganizing the college of medicine and surgery faculty for the purpose of reducing the number of clinical staff members and increasing the teaching efficiency of the college. All faculty members were requested to submit written resignations. On Jan. 11 Dean Wesbrook and all heads of departments complied. The remainder of the faculty promptly responded. On Jan. 15 he announced a further

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plan which consisted of appointing a reorganization committee composed of 3 members of the faculty and 3 graduates of the college practicing in Minnesota outside of the Twin Cities. The board of regents appointed President Vincent; the dean, F. F. Wesbrook; 2 members of the executive faculty, Dr. J. E. Moore and Dr. Charles L. Greene; and 3 alumni of the college, Dr. L. B. Wilson, Dr. E. L. Tuohy, and Dr. Theodore Bratrud. This committee was requested to present to the regents first a complete plan of organization for the medical faculty and, second, nominations of individuals to fill the positions provided in this plan. The report of the committee was received, revised, and adopted on Feb. 17, 1913, to take effect Aug. 1, 1913. Of the 184 faculty members only 70 were reappointed. Obviously, considerable ill feeling existed among the 114 whose appointments were not renewed. Moreover, the lower teaching ranks assigned to many of the faculty left an unpleasant reaction. Dr. Thomas Lee, who for many years was professor of anatomy and chief of the department, received the new title of professor of comparative anatomy, while the headship was awarded to Dr. C. M. Jackson, University of Missouri. Dr. C. A. Erdman, who had long been professor in charge of teaching gross anatomy, was reduced to associate professor of applied anatomy. Dr. E. Brown, who was professor of pharmacology and was anticipating the headship of that department, was reduced in rank to associate professor, while A. D. Hirschfelder, of Johns Hopkins University, was made head and professor of pharmacology. Dr. R. O. Beard, who was professor of physiology on the original faculty in 1888, became associate professor of physiology, while Dr. E. P. Lyon of St. Louis University became professor and head of the department of physiology.

In 1913 Dr. Wesbrook submitted his resignation to be effective July 1 as dean of the college of medicine and surgery of the University of Minnesota. He was to become president of the University of British Columbia. President Vincent knew E. P. Lyon at the University of Chicago and, knowing that he had been dean of the St. Louis University School of Medicine for six years, President Vincent was pleased to get him as dean at the University of Minnesota, in addition to the headship of the department of physiology. When Dean Lyon arrived and attended the first administrative board meeting on Sept. 8, 1913, the feeling of many clinicians in the Twin Cities who had resigned and had not been reappointed and those in the laboratory departments who had been demoted was still quite intense. The school was being bombarded by a number of physicians, many of whom were prominent practitioners of medicine and surgery in the Twin Cities. Thus, Dean Lyon, on the day he arrived, inherited the difficult problem of trying to bring a spirit of cooperation and peaceful coexistence out of a chaotic state. However, he had unquestioned support from President Vincent and most of the active members of the faculty. Moreover, further trouble loomed with the first mention by President Vincent of an affiliation of the medical school with the Mayo Clinic. As the storm clouds drew nearer and nearer, Dean Lyon found himself in the midst of an even more difficult problem than that which he found on arrival, incurred by reorganization of the faculty which President Vincent, with a committee from the faculty, had invited. Those who had resigned but had not been reappointed during the reorganization had not been completely reconciled. Moreover, for a number of years there had been developing an unfortunate attitude toward the Mayo Clinic among some of the Twin Cities physicians in private practice. Dr. S. Marx White called attention to some of the occurrences which resulted in this attitude. He pointed out that in 1905 McClure's Magazine published an extensive article entitled, "Modern surgery," by Samuel Hopkins Adams, a popular writer. Mr. Adams had visited Rochester and written a vivid account of the work of the Mayo brothers in a small rural community. He stated that in this private enterprise these two brothers and their staffs handled more surgical cases than any other hospital in the United States—even more than the Johns Hopkins Hospital. This article about the Mayo brothers and contemporary surgery evidently touched off a series of other articles in publications all over the country. Although this publicity was not solicited by the Mayo brothers, it created much indignity among medical men and surgeons, especially in the Twin City area, where it was looked upon as blatant advertising. It brought to the surface a resentment which had been growing here. Moreover, Dr. Thomas S. Roberts, a graduate of the University of Pennsylvania, who was professor of diseases of children in the medical school and also had a practice particularly among the prominent and wealthy citizens here, took most of his surgical patients, as did a few other physicians, to Rochester instead of employing surgeons in this community.

From the time President Vincent first mentioned an affiliation of the school of medicine and the Mayo Clinic, March 11, 1913, through appointment of a committee in March 1915, a colossal effort was waged by a few Twin City physicians against adoption of such an affiliation. By

action of the board of regents the affiliation was temporarily effected, but with the graduate school instead of the medical school. All of this had resulted in so much ill feeling that resignations were submitted even by some of the clinical faculty members. After declining the deanship in 1913, Dr. Charles Lyman Greene had continued as chief of the department of medicine. However, on June 12, 1915, his resignation was announced. On July 12, resignations were reported from Charles D. Freeman, G. S. Gilfillan, A. R. Hall, George D. Head, John B. Hynes, and J. L. Rothrock. Most of these physicians had been top-notch teachers and had worked without financial renumeration. Dean Lyon thoroughly understood the sacrifies they had made on behalf of the school and their value to the future of the school. Therefore, he arranged for a personal conference with them with the hope that they would reconsider. Only 2 men, Drs. Hall and Head, were willing to give further thought to their resignations, and only Dr. Hall remained on the faculty. On July 28, 1915, Dr. Moore, chief of the department of surgery, moved that the administrative board recommend to the president with regret the acceptance of the resignations. The motion was passed and the secretary was directed to send each of them a letter of regret concerning the severance of their relations with the school. All of this was very painful to Dean Lyon but he had done his best to convince them to continue on the teaching faculty. The 1915 temporary affiliation with the Mayo Clinic was replaced by a permanent union with the immediate transfer to the university of the endowment fund for the support of the foundation.

As long as President Vincent remained with the University of Minnesota no further outburst was made against the affiliation of the school with the Mayo Clinic. However, in March, after President Vincent announced his resignation on Jan. 31, 1917, a widely circulated pamphlet entitled, "Why the Mayo affiliation with the university should be terminated," appeared. This contained 12 reasons why the affiliation should be abandoned and was signed by 78 physicians residing in the Twin Cities, Duluth, and other parts of the state. This pamphlet was circulated also to members of the legislature. In the pamphlet earnest and active support was requested of a bill which had been introduced into the state legislature asking for discontinuance of the Mayo Clinic affiliation.

When Dean Lyon was alerted he promptly appointed Emil Geist, S. Marx White, and J. C. Litzenberg as a committee to formulate a reply. He then called a meeting of the general faculty on March 19, 1917, at which the committee presented its reply. In its final form this reply was sent to all members of the legislature, to the medical profession throughout the state, to the alumni outside the state, to THE JOURNAL-LANCET, and to the *Alumni Weekly*. The reply was published in THE JOURNAL-LANCET April 1, 1917, and the opposition to the affiliation failed. This entire situation was directed admirably by Dean Lyon.

Few men before or since could have gone through the trying ordeals of deanship as E. P. Lyon did from September 1913 to March 1915. He was in a position new to him which would have consumed all of the time of most deans. Added to this was the nerve-racking, time-consuming ordeal of defending the promotion of establishing a permanent affiliation with the Mayo Clinic. His vast store of knowledge, equanimity, forthrightness, sense of humor, and previous experience carried him through admirably.

In 1921 Dr. R. O. Beard said, "The foundation is, in itself, a magnificent conception. Its potentialities for good in the service of the public and in the promotion of medical education are unmeasured. But it remains a matter for the keenest regret that by reason of influences we cannot analyze, nor even comprehend, this great good should have been secured at so sad a sacrifice of some of the best teaching ability in the faculty and at the cost of so much of the goodwill of the alumni and of the profession of the state."

Dean Lyon continued to have criticism from time to time. There were those who believed that no person who did not hold a degree in medicine should be dean of a medical school. Soon after Dr. Coffman became president of the university in 1929, he recommended that a comprehensive survey be made of the school of medicine to make certain that it remain on solid ground. This survey was to be made by distinguished and disinterested representatives of the medical profession. On Jan. 6, 1921, on President Coffman's recommendation, the board of regents authorized the appointment of a special survey committee, consisting of Dr. Frank Billings, professor of medicine at Rush Medical College, Chicago; Dr. J. M. T. Finney, clinical professor of surgery in the medical school of Johns Hopkins University; and Dr. V. C. Vaughan, dean of the medical school of the University of Michigan.

This committee made a comprehensive investigation and after several weeks of study and conference submitted a most favorable report. They made suggestions and recommendations which they thought would strengthen the school.

The committee reported that during the investigation "some members of the faculty and some of the alumni think that the dean of a medical school should be a graduate in medicine and argue that because the present dean is not a medical man he is unfit to serve as dean of the medical school. The committee found no one who questioned the ability, the honesty, and the devotion to the work of the present dean. Your committee does not concur in this statement made by some of the individuals with whom the committee conferred that a clinical teacher only is qualified by that fact to efficiently fill the position of dean of a medical school."

On Nov. 2, 1921, after consideration of the report of the committtee on survey of the medical school, the administrative board unanimously voted its approval of the administration of Dean Lyon. They ordered that the secretary be instructed to transmit the statement to the *Alumni Weekly*, THE JOURNAL-LANCET, *Minnesota Medicine*, and the *Journal of the American Medical Association*.

Concerning this criticism of Dean Lyon, Dean Ford frequently countered by saying he regarded him as the best medical educator in this country. He was generally considered as an "open-minded, farsighted, clear thinking scholar —a leader among leaders of men." Moreover, Dean Lyon was held in high esteem and was admired and respected in educational circles in medicine.

In 1925 it was pointed out that when he became dean of the school of medicine it almost seemed there was a wall about the medical campus blocking it off from the rest of the university. During the next twelve years this was changed.

"We are now amalgamated into the greater whole. Our programs interdigitate with those of the other colleges. Hundreds of students from other colleges take subjects in the medical school and representatives of our departments sit on other faculties. We have come to realize the ideal that the medical school is not an organization alone for the training of physicians, but rather is the custodian and reservoir of the medical sciences; the mechanism for supplying instruction either as the basis for a profession or as a part of a general education; and, finally, that the medical school is the organization by which, through active research, these sciences may be forwarded and improved. I count this changed attitude of the medical school as one of its finest achievements of the last ten years."

When Dean Lyon came to the University of Minnesota the graduate school of medicine idea was sprouting. He promoted the giving of graduate degrees in clinical subjects so that it became known as the "Minnesota idea." Soon after he arrived, proposals were submitted for the creation of teaching fellowships under the ordinary relation of a graduate school in medicine in association with the medical school. A committee was appointed which recommended that the degree of master of science in surgery be offered; such fellowships became available in the various departments. This work carried on until the degree of doctor of philosophy was also being offered in clinical subjects and was greatly stimulated with establishment of the Mayo Foundation. Literally hundreds of such degrees have been conferred by the graduate school for work in clinical subjects. Thus, for approximately twenty-three years, Dean Lyon vigorously promoted graduate work in all departments of the school of medicine.

As soon as possible after assuming his position at the University of Minnesota, Dean Lyon began to develop plans for full-time clinical professors. Practically all faculty members in the laboratory department were already on full-time basis. When Charles Lyman Greene resigned as chief of the department of medicine on June 12, 1915, Dean Lyon promptly urged that he be replaced by a full-time chief. A provision was made whereby Dr. L. G. Rountree of Johns Hopkins University was employed on practically a full-time basis, with restricted consultation practice, but no private office off the campus.

At a meeting of the administrative board of the school of medicine on Feb. 18, 1918, Dr. J. P. Sedgwick, chief of the department of pediatrics, desired to be considered for full-time chiefship. Dean Lyon appointed a committee to thoroughly investigate the subject again and to make recommendations as to just what was to be required of a full-time clinical chief. A committee was appointed with Dr. A. D. Hirschfelder, head of the department of pharmacology, as chairman. This committee produced a long comprehensive report which did not meet with entire approval of some members of the board. On April 9, 1918, Dr. Hirschfelder's committee presented a supplemental report, parts of which were combined with the original report, resulting in requirements for full-time chiefs. It met the approval of the administrative board and all concerned. Thus, Dean Lyon's plan had succeeded. This, with slight modifications from time to time, has been continued not only in regard to chiefships but also to many other teachers in clinical departments.

Miss Catherine J. Densford said, "In later years, when upon Dr. Richard Olding Beard's retirement, Dean Lyon became more actively

responsible for the development of nursing education in the University of Minnesota, on the half-century old problems of nursing he now turned his keen analytical mind and with unerring eye, with his finger directly upon the fundamental weakness of nursing education, it was he who issued the clarion call which brought for the first time a nationwide realization that the profit motive must be taken out of nursing education if nurses are to be prepared for community service."

Dean Lyon was always most considerate in recognizing others who had been helpful to him. For the first twelve years of his deanship, Dr. Richard Olding Beard was assistant dean of the school of medicine. At the time of Dr. Beard's retirement in 1925, Dean Lyon listed some of the outstanding accomplishments of that period, then, he said, "I can truthfully say that not one accomplishment, not one advance, not one plan, of these twelve years but has been largely influenced, shaped and invigorated by Doctor Beard. We trust that he may long remain with us as a counsellor and friend, and that he may live to see the medical school whose small beginnings he witnessed and fostered, whose middle years he so largely helped to formulate and guide, become the great institution for good which his genius foresaw and his labors hastened. May he live in health, strength and happiness to see this consummation of his labors; and in that day, even as now, may he feel the acclaim of his thousands of students and his hosts of friends for one who honors and is honored by the choicest epithet: He was a teacher—a teacher of men!"

Dean Lyon was a true friend of students and young staff members. He had an ability far beyond that of most persons to evaluate the qualities of young teachers. He took great pride in referring to O. H. Wangensteen and pointed out that he was chosen to become the head of the department of surgery and was provided with a stipend of $2,400 for a year of foreign study in preparation for later assumption of the duties of the headship. Two other young men, in whom he and his co-worker saw great potentiality and chose them to head departments at a later time, were Dr. Leo G. Rigler and Dr. J. C. McKinley. After special training in various parts of the world they returned and received their headships. Dr. Rigler developed one of the finest departments of roentgenology anywhere, and Dr. McKinley headed the department of medicine and later the division of psychiatry with outstanding contributions. In citing these and other cases, about the time of his retirement, Dean Lyon said, "State institutions aren't supposed to do things like that but private ones can. But we did it."

In the 1930s it was said that Dean Lyon had the youngest faculty members of any medical school in the United States.

From 1913 to 1937 Dean Lyon published more than 80 articles in medical, nursing, and educational journals, 4 of which were published in 1936. Being a physiologist he was especially interested in conditioning air. He wrote a number of articles in this field, the first being "Tests of radiator humidifiers" which was published in *Science*, 1917. Another article the same year was entitled, "Requirements for radiator humidifiers," which appeared in *Heating and Ventilating Magazine*. In 1918 he wrote on the problem of "Humidity indoors" for *Minnesota Medicine*. In 1920, the "Effects of breathing dry and moist air" appeared in the *American Journal of Physiology*. "How to put humidity in your home" was published in *Hygeia*, 1926, and "Humidity in the home" appeared in *Hygeia*, 1931. He also wrote on a variety of other subjects. Among his articles published in 1936 were "I am automatic" for THE JOURNAL-LANCET and "Swans sing before they die" for the *Journal of the American Medical Association*. This was presented before the Congress of Medical Education. He pointed out that this title was only a partial quotation and that the full stanza was:

> Swans sing before they die,
> 'Twere no bad thing
> Did certain persons die
> Before they sing

He said, "I suggest the hypothesis that I had in mind, the latter part of the verse rather than the doubtful biology of singing swans." This article which was published in the April 1936 issue of the *Journal of the American Medical Association* is well worth reading by the medical profession of today.

During Dr. Lyon's deanship a number of buildings were constructed, beginning with a hospital service building, connected to Elliot Memorial Hospital Building in 1915, the Todd Memorial Hospital in 1924, the George Chase Christian Memorial Cancer Hospital in 1925, the Minnesota Hospital and Home for Crippled Children in 1928, the new health service building in 1928, the outpatient department in 1929, the medical science building in 1932, which was later known as Owre Hall, and the psychopathic hospital in 1936. For many years he had continued efforts to procure an adequate building for the school of nursing which was constructed in 1933 and later named Powell Hall.

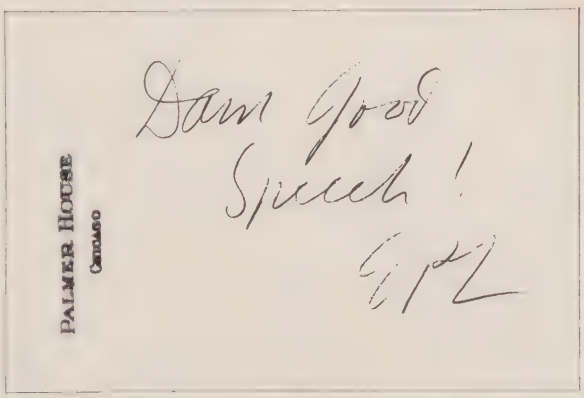
It was my good fortune to come under Dr. Lyon's deanship in the fall of 1914 as an instructor in anatomy, with permission to carry a few subjects each quarter in the school of medicine. Within a few weeks after our family arrived we were pleasantly surprised when Dean and Mrs. Lyon and Dr. and Mrs. C. M. Jackson appeared to make us a visit in our $20 per month abode. They had come not only to see that we were comfortably located but also to take us on a tour of the city of Minneapolis. The kindness, goodwill, and encouragement offered that afternoon were so pleasing and impressive that today our memories of that pleasant afternoon are just as vivid in our minds as they were fifty years ago. Dean Lyon continued to manifest that same kindliness and helpfulness in guiding me through the medical school while an instructor in anatomy. He approved the promotion to assistant professor in 1923, associate professor in 1926, and professor in 1932. The expressions of encouragement at every step of the way and his same watchfulness and guidance continued until he retired by reason of age in 1936. Thus, during his twenty-three years as dean, I had the good fortune to be under his direction for twenty-two of them. During those years, I felt as free to go to his office for counsel and advice as to go to my own home. At no time did he manifest the slightest degree of impatience regardless of how busy he might be with other items. From the dozens of such visits at his office I always came away encouraged and enlightened. This was not a special privilege which only I enjoyed but it belonged to everyone in the school, students and faculty alike. This was one of the qualities that caused him to be so admired and loved as a dean. In addition to such office conferences we had considerable official correspondence. When we were to have a guest physician from this country or abroad, especially interested in my field of activity, a letter would be sent to Dean Lyon asking if a special lecture to the students and faculty might be arranged. Almost without exception he made special arrangements for such lectures requesting that other classes be dismissed during that hour and often providing the lecturer with an honorarium from the medical school.

Dean Lyon's replies to letters were nearly always short and to the point. He wasted no time in verbosity. Often he even indicated his reply in longhand on the letters and then returned them. A good example of this is a letter in which two items were involved; one was whether a science writer could quote rather extensively from one of his recent published articles. In the margin of the letter he wrote, "Tell her o.k." The other was concerning a physician who was anxious that the dean write an article for a certain publication. In the margin he wrote, "Yes, I'll do it."

On Oct. 15, 1931, he and I were scheduled to speak on the program of the Illinois State Nurses' Association in Chicago. He had kindly invited me to share a hotel room with him. In the afternoon he was scheduled to take a train to New York. He had spoken but had to leave for the station a few minutes before my part of the program was completed. He had gone back to the hotel room and on a small sheet of Palmer House stationery he had written the following, "Dam good speech! EPL" (see figure). These three words, initialed, meant more to me than any long letter he might have written. Dean Lyon's originality was supreme. One year, about a week before Christmas, his many friends received a penny postcard on which every bit of space on both sides except for the address and Dean and Mrs. Lyon's signature was covered with tuberculosis Christmas seals. He later explained that instead of buying expensive Christmas cards, he and Mrs. Lyon had decided to spend all but one cent on seals for each of their friends. My last letter was received from Dean Lyon under the date of June 11, before he retired on June 30, 1936.

Dean Lyon had a sense of humor that stood him in good stead on practically every occasion. He had an appropriate witticism for every situation. His laugh was contagious.

His famous "William Beaumont Cottage" was on the St. Croix River in Prescott, Wisconsin, some 30 miles from the University of Minnesota, where during the spring, summer, and fall months Dean and Mrs. Lyon spent weekends. They nearly always had guests. It is doubtful that an invitation to spend an afternoon, an evening, or a weekend at "Beaumont Cottage" was ever declined. Hundreds of friends still



visualize Dean Lyon in his characteristic summer cottage garb, making conversation with a spirit that made everyone feel a member of the family.

When Dean Lyon attained retirement age a testimonial dinner was given in his honor on June 10, 1936. At that time Dean Harold S. Diehl presented a portrait of Dean Lyon to Dr. W. J. Mayo for the board of regents. It was announced that an Elias Potter Lyon Lectureship had been established. On that occasion President Coffman said, "Dean Lyon was never actuated by mean or selfish motives. He was kindly and generous in dealing with others, professional and high-minded in discussing the problems of the medical school and friendly to the students and staff. In his administrative capacity he kept his face to the future rather than to the past. A scientist in his own right, he knew how to evaluate the scientific efforts of others. He has been a university dean who administered the affairs of his college with no thought of gain to himself, and in a spirit of selflessness which others would do well to emulate, and his contribution to the university is as enduring as the benefits of medical science are to humanity, Dean Lyon!"

That night Dr. W. J. Mayo said, "When Doctor Elias P. Lyon came to the university twenty-three years ago as professor of physiology and dean of the medical school, the teaching of medicine in Minnesota was of a clinical type, with only moderate scientific background. Today the medical school of the University of Minnesota, clinically and scientifically, is one of the first ten medical schools in America." In response Dean Lyon said, "Mind, you, I'm not ashamed of my job, but I think it has been only a small part of the much larger job we have done together. Minnesota's medical school is a first-class institution. It is no one man's monument. It stands for all who have worked here, from Millard, first dean, to the last teaching fellow."

During his retirement year he said he had lived through the most interesting time anyone could possibly have lived. He also said that harmony in the faculty is the most necessary thing in a medical school—and the most difficult to get. "But we got it." He said that when a new professor was chosen, he did not act as czar; it was done by group action of department heads.

Dean Lyon's loyalty to the school of medicine was unsurpassed. On Dec. 18, 1930, he informed the board of regents that he was making the university the beneficiary of his group life insurance. Unstintingly he gave twenty-three years of his life to this institution.

After retiring on June 30, 1936, Dean and Mrs. Lyon decided to spend the next winter in Florida. On their way back to Minnesota, on May 4, 1937, while driving through the mountains, he told Mrs. Lyon that he did not feel well and askel her to drive. He died soon after reaching a hospital at Trafford, Pennsylvania.

Dr. Anton J. Carlson, professor of physiology, University of Chicago, gave the first Elias Potter Lyon Lecture at the fiftieth anniversary of the founding of the medical school in October 1939. He said, "The University of Minnesota entrusted Dean Lyon with an almost superhuman task; namely, the leadership of the then preadolescent medical school and the leadership of the important department of physiology. These are all-day jobs for two superior men. That Dr. Lyon carried these two responsibilities with the results now in evidence speaks volumes for his industry, his wisdom, his gift of leadership, and his sense of humor. Elias Potter Lyon may not rank with the giants of the earth especially in medical research, but his conspicuous unselfishness, his industry, his sense of justice, his never-failing kindness, and his salty but kindly humor are worthy qualities challenging us all."

In the early 1950s the institute of anatomy and Millard Hall were connected by a laboratory research building which was appropriately named Lyon Laboratories. At the dedication ceremonies on Feb. 11, 1954, Dean Harold S. Diehl said, "In medical education, Dean Lyon long occupied a position of national leadership. He had the vision of new horizons and the courage to depart from traditional methods, yet, he was always wisely conservative. He left enduring footprints in the sands of medical education, and his imprint indelibly upon this medical school. This is in the records, but to the students who were privileged to know him, Dean Lyon's outstanding qualities were those of kindliness and personal human interest. He always considered the welfare of the student of first importance, and helped many a one over the rough spots on a road to a medical career. And so a decade and a half after his death we can say of Dean Lyon that the shadow of his accomplishments and influences have lengthened rather than shortened with the passage of time."

In his dedication presentation Dean Diehl used the following quotation:

> A king once said of a prince struck down,
> 'Tis taller he seems in death:
> And this speech holds truth for now as then,
> 'Tis after death we measure men.

Since this statement by Dean Diehl, another decade has passed with continued lengthening of the shadow of Dean Lyon's accomplishments.

Transactions of the North Dakota State Medical Association

SEVENTY-EIGHTH ANNUAL MEETING

Grand Forks, North Dakota, May 1, 2, 3, and 4, 1965

(Continued from the August 1965 issue)

PROCEEDINGS

House of Delegates, Second Session

Grand Forks, North Dakota — May 2, 1965

Speaker Christoferson called the meeting to order at 2:00 P.M. at the Dacotah Hotel at Grand Forks, N.D.

Dr. Skjei, Chairman of the Committee on Credentials, reported that there was a quorum present.

Secretary Buckingham called the roll and the following delegates and alternates responded:

Drs. H. A. Norum, Fargo; C. K. Fercho, alternate, Fargo; A. C. Burt, Fargo; R. E. Kulland, West Fargo; Paul Beithon, Wahpeton; J. V. Sessums, alternate, Fargo; R. J. Ulmer, Fargo; G. H. Hilts, Cando; R. D. McBane, alternate, Devils Lake; L. T. Longmire, Devils Lake; R. C. Painter, Grand Forks; J. A. Sandmeyer, Grand Forks; G. L. Countryman, Grafton; W. T. Powers, alternate, Grand Forks; L. A. Giltner, Minot; A. M. Cameron, Minot; Jens Sahl, Minot; Warren Jensen, Valley City; P. O. Dahl, Bismarck; J. J. Moses, Bismarck; R. B. Tudor, Bismarck; M. A. K. Lommen, Bismarck; C. J. Baumgartner, Bismarck; E. G. Vinje, Bismarck; E. O. Hieb, Jamestown; J. V. Miles, Jr., alternate, Jamestown; D. E. Skjei, Williston; W. C. Hanewald, Dickinson; R. E. Hankins, Mott; J. M. Little, Mayville.

There were thirty delegates and alternates present. Others attending were:

Drs. G. A. Dodds, Amos Gilsdorf, E. H. Boerth, C. H. Peters, G. W. Toomey, R. D. Nierling, Keith Foster, G. Christianson, J. D. Craven, C. J. Glaspel, Dean Strinden, R. E. Mahowald, R. W. McLean, F. A. DeCesare, W. R. Fox, J. M. Van der Linde, Mr. L. Limond and Mr. S. Williams.

As the first order of business Speaker Christoferson introduced Mr. Sherwood Williams, Field Representative, American Medical Association. His remarks follow:

"Since Dr. Wright briefed you yesterday on legislation, I will not go into this. I would like to commend you on your legislation educational campaign. While on the surface, it may look like all was lost, it is not so.

"I would like to tell you a little about the Field Service and what a Field Representative is, and what he is to do. This field service was set up about eight years ago. There are twelve of us now in the United States. We each have four or five states to cover. I have North Dakota, Montana, Idaho and Washington. There is an International Field Representative who does the same work as we do with the various states and with other countries. The field representative acts as a basic liaison officer with the county medical societies. Most of our work is with the executives of these county medical societies. Our business is to keep the committees up to date on what the various programs are which are thought up by the Councils and Committees of the AMA. Sometimes I think the most important of our functions is actually discovering the problems each state has and transmitting this information from one state to the other. Basically, you all have the same problems. Sometimes one state comes up with an answer.

"Sometimes we are accused of knowing everything about everything. This is not so, but we do know the individual in the AMA with whom you may get in touch to get certain facts and information. The American Medical Association is your organization, and I urge you to learn about it and about the services it has, and use these services.

"Along the way if I can be of any help, please do not hesitate to contact me."

Since there was no objection, the reading of the minutes of the first session was dispensed with. Speaker Christoferson introduced Mrs. Smith, president, Woman's Auxiliary.

PRESIDENT'S ADDRESS WOMAN'S AUXILIARY

MRS. CLYDE SMITH: From the day an Auxiliary member is asked to be Second Vice-President of the Woman's Auxiliary, she spends the next four years both looking forward to and dreading this moment. And now at long last my moment is here and I can scarcely believe it. But I intend to make the most of it. The chance to have the undivided attention of a roomful of handsome and intelligent men is too wonderful not to appreciate thoroughly.

I am the nineteenth doctor's wife who has had the great privilege and the high honor of speaking to this distinguished group. We have come in assorted shapes, sizes and ages with various talents, interests and accomplishments, but we share a deep devotion—our interest in furthering the ideals of the American Medical Association and our dedication to the fight to preserve our husbands' right to practice as free Americans.

As I am both the wife and the mother of a doctor, I am doubly determined to fight with every means at my disposal so that the day may never come when they are pathetic placard-carrying strikers like their colleagues in Belgium and England, begging for a decent wage and a chance to practice with integrity and freedom. You can be sure that 86,000 members of the National Auxiliary are as one in this regard. Our Legislative Chairmen are tireless in their efforts to educate both doctors' wives and the public of ever-spreading government control.

My purpose here today is two-fold; to brag and to beg. I am extremely proud of the activities of the Woman's Auxiliary to the North Dakota State Medical Association. I'll give you briefly some of the accomplishments of this wonderful group, more or less in alphabetical order.

This year we have increased our contribution to the

American Medical Association Education and Research Foundation, from $500.00 which we gave last year to $1,157.00 We feel this is one of the best ways we can combat increasing government spending and interference in the field of medicine.

I nearly burst with pride when one of the North Dakota Auxiliary members was chosen to represent all Community-Service-Minded members in a wonderful article in our National Bulletin. Marilyn Swenson of Jamestown was featured in the article called "The Rewarding Life of Marilyn Swenson." She is a beautiful and charming girl and an excellent representative to show off on a national scale.

Like Marilyn, many other Auxiliary members have served their communities in myriad ways for an astronomical number of hours. In my own district, for example, members have served as city chairmen for the Community Chest Drive, Heart Fund and Cancer drives, and as chairmen of the County Mental Health Association. Church work, P.T.A.'s, Scouts (both boy and girl), immunization clinics, Christmas baskets for needy families, parties for crippled children, and senior citizens, have been some of the reasons dinner may have been late in your home sometimes during the past year.

International health activities are receiving our enthusiastic support. Last year we mailed 18 cartons of sample drugs and a used EKG machine to be used by doctors overseas, thanks to you doctors. This year we have included bandages rolled from sheets—some from our own beds and some scrounged from hospitals, hotels and motels, as well as soap scraps from the same sources.

We have an excellent Health Careers Chairman, with several active groups in the state. They have speakers on many medical fields, tours, demonstrations and volunteer hospital work in their program. A successful state rally was held in Jamestown last year and one is planned for Minot this fall.

Our Mental Health Chairmen have been active in promoting the radio series called "Mirror to the Mind"—a series of 13 half-hour discussions on various phases of mental health. Several stations have used, or are using, this program and we hope all parts of the state will be covered during the coming year with "The Cry for Help."

Our Student Loan Fund stands as one of our finest accomplishments. The net worth as of last year was $29,100.00. When our contribution for this year of around $2,000.00 is added, we shall be well over the $30,000.00 mark. The loans are made in amounts from $500.00 to $1,000.00. We ask only 2½% interest, so our loan is popular and is always completely loaned out.

There are many other wonderful programs which our National Auxiliary maintains such as: homemaker services; baby sitter training courses; health education material distribution (posters and pamphlet racks); safety programs; disaster preparedness; medical self-help programs—are all among the National activities we try to support to the best of our ability though we are handicapped by our small numbers.

I have come to the end of my bragging, and now I must beg.

There is a dark side to the Auxiliary picture. We are on the verge of financial disaster. This year we have had a decline in membership from 332 to 309, with an ensuing loss in dues.

Last year the North Dakota State Medical Association membership was 449—ours 332. This year your group was 455—ours 309, which is still a respectable 68% compared to National Auxiliary membership of 86,127, and American Medical Association membership of 203,000. We seem to be in good shape—I don't know where. However, for a state like Ohio, or California to have less than half of the potential membership does not hamper their activities. They still have between five and ten thousand members. Our budget at $3.00 per member for state dues will have scraped through the bottom of the barrel. Last year our budget was cut to the very bone and came to $1,109.00. This year our $927.00 will not be adequate to function properly.

We are a mature, hardworking group with serious commitments—long past the stage of ice cream socials and chats over teacups. Our budget covers these essentials:

President's Fund:		
National Convention	$250.00	
Chicago Conference	120.00	
Expense Fund	125.00	$495.00
President-Elect's Fund:		
Chicago Conference	120.00	120.00
Other Funds:		
Committee Chairmen	60.00	
News, Views and Cues	250.00	
Past President's Pin	9.00	
A.M.A.E.R.F.	25.00	
S.A.M.A.	100.00	
Miscellaneous Fund	50.00	494.00
Total		$1,109.00

Each and every one of these items is justified and is budgeted at the lowest possible figure. It is essential for the President and President-Elect to attend National Conferences and Conventions for their enlightenment and inspiration. Contact with the many wonderful women who make up the Auxiliary from all over the country is a marvelous experience and leads one to the conclusion that doctors have excellent taste in their choice of wives. Another reason we must provide these travel opportunities is an incentive to get a busy and competent woman to take on the task of the State Presidency. It does take time and the president's lot is not always a happy one.

Our little news publication, News, Views and Cues, is a vital link in our chain of communication. It has been a miracle of economy—only $50.00 per issue. Our present editor, Audrey Mahoney of Devils Lake, is resigning, so we shall have to find a new printer and probably a more expensive one.

There is a solution to our financial problem and it is already in operation in five small population states—Montana, Idaho, Utah, Nevada and Arizona. This is the team-membership approach. In other words, the doctor pays his wife's dues when he pays for his society membership. The following item appeared on page 7 in the March-April issue of "PR-Doctor," a publication of the American Medical Association:

At the 1964 Clinical Convention, the AMA House of Delegates took note of the Auxiliary's past accomplishments and passed a resolution urging "each state and local medical society to support fully and to aid and encourage the Woman's Auxiliary to the AMA in all its endeavors, particularly in the joint husband-wife project."

In this state the dues would amount to $5:00; $2.00 to National and $3.00 to the State Auxiliary. If a doctor's wife wishes to do so, she may decide not to join her district auxiliary—those dues are usually $1.00 per year. But we are hopeful that all doctors' wives who realize that they are state and national members will want to become active on the local level because that is where our accomplishments take place.

It is rather ironical that you men seem to find us women rather fascinating one by one—but unthinkable in organized groups. The Medical Auxiliary is not just an-

other woman's club; we ask that you not keep us ladies-in-waiting. Let us keep helping you obtain your objectives in medicine.

So now we face our present situation here in North Dakota. It is a sort of Ogden Nash's definition of incompatibility—you have the income, we have the patability. In order to keep this happy state of affairs, we ask you—we implore you—to take official action upon our modest request that North Dakota adopt the team-membership approach to solve our budget problems with, we hope, the desired side effects of having some wives who are now inactive find some worthwhile project in the Auxiliary and then join us in work on that project.

We feel that if the House of Delegates goes on record approving the team-membership plan and forwards a copy of this approval to each district, it will be of great assistance to our membership chairmen when they will be asked to approach each local group to request them to adopt this joint-membership plan.

At the request of our State Board which met last fall and approved team-membership, I hereby present a formal request that the House of Delegates bring this matter to the floor for consideration and, we hope, favorable action.

Our National Motto this year is "Better Health—Better World." All we ask is that you help us give more of your wives a chance to assist us in reaching this goal.

Gentlemen, thank you for asking me to come here today. Perhaps now you are sorry that you did. I sincerely appreciate this chance to speak to you, and I am looking forward to seeing you all tonight under gayer circumstances at the mixer. Until then—Auf Wiedersehen.

Speaker Christoferson expressed the appreciation of the House to Mrs. Smith for her very fine presentation and then directed the Secretary to read the letter, and its enclosure, addressed to the House of Delegates from the Woman's Auxiliary.

Secretary Buckingham read the following letters:

(Letter to Dr. Dodds, President and Dr. Lee Christoferson, Speaker—May 2, 1965)

Gentlemen:

The Woman's Auxiliary to the North Dakota State Medical Association respectfully requests the House of Delegates to bring to the floor for discussion the joint husband-wife membership plan.

Will you please read the enclosed letter addressed to Dr. Vinje as it is a sample of the letter all district presidents will receive in the near future about this matter.

We are hopeful you will consider this idea favorably and will recommend its adoption to your component societies.

ss Mrs. Clyde Smith, *President*
Woman's Auxiliary

Letter to Dr. R. Vinje, President, Sixth District Medical Society, Bismarck, N.D., April 12, 1965

Dear Doctor Vinje:

The Woman's Auxiliary to the American Medical Association has proposed a "team membership plan" to bring the Auxiliary membership to 100% of the American Medical Association's membership. This plan will close the existing gap in the relative membership.

The "team membership plan" is that the M.D. when paying his dues at the County level include those of his wife for State and National Auxiliary. The National dues are $2.00, one of which includes subscription to the official organ—"The Bulletin"; and the North Dakota State dues of $3.00—a total of $5.00 per year.

Five states now have 100% in this team-membership plan. They are Montana, Idaho, Utah, Nevada and Arizona.

How does the membership in the Woman's Auxiliary to the North Dakota State Medical Association compare to the membership in the North Dakota State Medical Association this year? On April 1, 1965 there were 455 regular members in the North Dakota State Medical Association compared to 303 Auxiliary memberships. Compared to last year's figures of 449 and 332 respectively. This indicates a relative drop of 7% in 1964-65 Auxiliary membership.

What is the picture in Sixth District? The membership in Sixth District Medical Society as of April 1, 1965 was 80; the membership in Sixth District Medical Auxiliary was 53; a gap of 27 memberships.

From the *Report on Actions* of the House of Delegates, American Medical Association, Eighteenth Clinical Convention, November 29-December 2, 1964, Miami Beach, Florida—"urged strong support of the Woman's Auxiliary and asked the state and county medical societies to give serious consideration to the idea of joint husband-wife membership."

In addition to showing an increased membership, a better state and national picture, it also presents a better basis for the planning of the Finance and Budgeting Committees, both at State and National levels.

National has indicated that this plan should begin at the local level. For this reason we have presented this information to you and to ask if you will inaugurate this "team-membership plan" in the Sixth District Medical Society.

ss Mrs. Clyde Smith, *President*
Mrs. M. A. K. Lommen, *Membership Chairman,*
Woman's Auxilary

After the reading of the letters, Speaker Christoferson stated that the Chair would entertain a motion for a recommendation to the Council, for their approval, that the dues for the Woman's Auxiliary be included in the regular billing of the dues for the State Association. It was so moved by Dr. Tudor, seconded by Dr. Hanewald. Motion passed.

Reference Committee to consider the reports of the President, Secretary, Executive Secretary, and Treasurer.

Dr. Little, chairman, presented the following reports and their discussions, which were adopted section by section and as a whole:

1. Report of the President. The Reference Committee reviewed and approved the report of the President with the exception that the President-elect be allotted up to $600.00 for travel expenses incurred, at the discretion of the Council, with the further exception that the Fifty Year Awards be left as is, and that no consideration be given to making this award at forty years after graduation from medical school. This portion of the report was adopted.

Dr. Little further moved that an Area-Wide Hospital Planning Committee be formed whose function will be to establish a voluntary effective area-wide hospital planning agency as a Special Committee of the State Medical Association, and further moved that the official representative on the Blue Shield Board of Directors have his report published in the Delegates Handbook.

During the discussion that followed, the question was raised as to the possibility of any conflict that might come with the Governor's Health Planning Committee.

Dr. Little explained that the proposed committee, at the suggestion of Dr. Dodds, would have as its function reviewal of a request by a city for a hospital. Dr. Little explained further that the Committee could only recommend its approval or disapproval of the need for a hospital.

Dr. Dodds pointed out that the Governor's State Health Planning Committee does not necessarily deal with this matter. He added that in some states the government has taken over that authority and he felt that the Medical Association should have some voice in this, and with an organization already in operation these problems could be dealt with as they arise, not necessarily through legislation. He explained that the Committee would have no power, but would act in an advisory capacity.

The question was raised by Dr. Ulmer as to whether administrators of hospitals should be included on this committee. Dr. Dodds stated that he felt that the committee should encompass those dealing in the field of

hospitals and administration—both at state and local levels.

Speaker Christoferson pointed out that in New York state, no longer can anyone, under any circumstances, build a hospital without specific legislation. He added that "it handicaps anyone from the free enterprise system of building a new hospital if they so desire. The method of this motion is to circumvent this. We are anticipating that this state might put some clamps on building new hospitals and we should have an informed committee as to utilization of beds and needs. If such a trend becomes present, we will be in a position from the standpoint of organized medicine to take leadership. This committee will not serve any function except in case such a situation arises."

Dr. Miles noted that perhaps, if osteopaths gain full practice qualifications in North Dakota, this could be another way of controlling requests to build hospitals by osteopaths.

Dr. Kulland suggested that any physician belonging to the North Dakota State Medical Association who desires to back a new hospital present this for consideration to the committee.

Dr. Little's original motions were passed.

The motion was made by Dr. Ulmer, seconded by Dr. Lommen, that the President of the North Dakota State Medical Association, with the advice and cooperation of the North Dakota Hospital Association, seek to establish a state-wide hospital planning committee. This motion passed.

2. Report of the Secretary. This report was reviewed and approved. This portion of the report was adopted.

3. Report of the Executive Secretary. This report was reviewed and approved. This portion of the report was adopted.

4. Report of the Treasurer. This report was reviewed and approved. This portion of the report was adopted.

The motion was made by Dr. Little, seconded by Dr. Hankins, that the report as a whole be adopted. Motion carried.

DR. JAMES LITTLE, *Chairman*
DR. JAMES J. MOSES, *Vice-Chairman*
DR. RICHARD H. LEIGH
DR. L. T. LONGMIRE
DR. R. E. KULLAND

Reference Committee to Consider the Reports of the Council, Councillors, and Special Committees

Dr. Countryman, chairman of this committee, presented the following reports and their discussions, which were adopted section by section, and as a whole.

1. Report of the Chairman of the Council. The report of the Chairman of the Council was perused and the following observations noted:

At the meeting held Saturday, May 2, 1965, in Minot, we commend the Council's action for inviting the Medical Students to observe the Interim Session of the Council held in Fargo, December, 1964.

We commend the Council's action of Medicare renegotiation.

We would like to emphasize the Council's suggestion that the Woman's Auxiliary avoid alliance with the Federal Loan Fund in the dispersement of their student loan fund.

Our Committee is strongly in favor of Tetanus Immunization Week, and we have submitted a Resolution to the appropriate committee.

In reviewing the report of Dr. Mahowald, Chairman of the Council, we commend him on his report and its completeness.

This portion of the report was adopted.

Your reference committee has reviewed the reports of the Councillors of all ten districts, and commend their thoroughness. We note with interest the Resolution submitted by the Second District Society regarding the staffing of the State Capitol Aid Station during the legislative session. We favorably considered this Resolution and referred this to the Resolutions Committee for action.

This portion of the report was adopted.

2. Report of the Committee on Cancer. This report was reviewed and approved. This portion of the report was adopted.

3. Report of the Committee on Nursing Education. The committee reviewed and approved the report in principle, with the exception of Item C, on Page 88 of the Handbook. It was felt by the committee that the ordering of types of fluids and medication to be administered by the nurses is the prerogative of the individual doctor, rather than the hospital or its administration. This portion of the report was adopted as amended.

4. Report of the Committee on Maternal and Child Welfare. The committee reviewed and approved the report with interest, and urged the continuation of the PKU examinations. This portion of the report was adopted.

5. Report of the Committee on Foreign Trained Physicians. The committee reviewed and approved the report, and commended Dr. Glaspel for his endeavors. This portion of the report was adopted.

6. Report of the Committee on Mental Health. This report was reviewed and approved. This portion of the report was adopted.

7. Report of the Committee on Diabetes. This report was reviewed and approved. This portion of the report was adopted.

8. Report of the Representative to the Crippled Children's Services Division of the Public Welfare Board of North Dakota. This report was reviewed and approved. This portion of the report was adopted.

9. Report of the Committee on Aging and Rehabilitation. This report was reviewed and approved. This portion of the report was adopted.

10. Report of the Liaison Committee to the North Dakota State Bar Association. This report was reviewed and approved. This portion of the report was adopted.

11. Report of the Liaison Committee to the North Dakota State Dental Association. This report was reviewed and approved. This portion of the report was adopted.

12. Report of the Committee on Pharmacy. The committee reviewed the report and recommended that the Committee be continued for the ensuing year. This portion of the report was adopted.

13. Report of the Committee on Liability Insurance. This report was reviewed and approved. This portion of the report was adopted.

14. Report of the Committee on Emergency Medical Service. This report was reviewed and approved. This portion of the report was adopted.

15. Report of the Committee on Medicine and Religion. This report was reviewed and the members of the committee commended for their activities. This portion of the report was adopted.

16. Report of the Committee on Constitution and By-Laws. This report was reviewed with the recommendation that this committee be continued for another year, as suggested by the Chairman of the Committee, Dr. Gilsdorf.

DR. COUNTRYMAN: At the House of Delegates meeting

in Minot in 1964, the following Resolution was presented:

Whereas, according to the By-laws of the North Dakota State Medical Association, the Councillor shall be elected by the House of Delegates, and,

Whereas, the Fourth District Medical Society believes that this method of selection could be improved,

Now, Therefore, Be It Resolved that the selection of a Councillor be made from a list of candidates given by the individual district societies.

After some discussion by the delegates, the following motion was made by Dr. Dahl, seconded by Dr. Larson, and passed:

I would move that the Resolution of the Fourth District Medical Society be submitted back to the ten individual districts for their action, to be brought up again a year from now at the next meeting.

DR. COUNTRYMAN: Having considered this Resolution, and polling the districts individually, the Reference Committee recommends the passage of the Resolution as stated above. This portion of the report was adopted.

Speaker Christoferson asked for discussion, explaining that many of the district societies did not vote on this resolution as such. He felt that this was the fault of the delegate to his particular society. The Speaker read the resolution again, pointing out that the Nominating Committee would be obliged to submit the names of the candidates for councillors from each district to the House of Delegates. After considerable discussion, Dr. Christoferson asked for a standing vote. In favor, 23; opposed, 9. Resolution passed.

SPEAKER: "The By-Laws, Chapter 14, are hereby amended. I will have to ask for a motion that this be inaugurated in 1966, by virtue of the fact that the local societies do not have sufficient time to bring in a list of candidates for councillor for the 1965 election." Motion passed.

Dr. Countryman moved that the report be adopted as a whole. The motion was seconded by Dr. Lommen. Motion carried.

DR. G. L. COUNTRYMAN, *Chairman*
DR. M. H. POINDEXTER, JR., *Vice-Chairman*
DR. JENS SAHL, JR.
DR. M. A. K. LOMMEN
DR. JOHN SESSUMS

The meeting was reconvened after a recess of fifteen minutes.

SPEAKER CHRISTOFERSON: There has been considerable discussion about this Resolution that was just passed. I would like to call your attention to what is resolved—that the selection of the councillor may be made from a list of names submitted by each district society. In any event, this is concerned only with the nomination of the councillor, as covered in Chapter V, Section II of the By-Laws, which reads as follows: "At the first meeting of the Annual Session of the House of Delegates, a nominating committee of three shall be appointed which shall submit its report to the House of Delegates at the Second Session of the House of Delegates."

My interpretation would be that we would have to make an addendum to the By-Laws, stating that in the case of councillors, the selection of the nominees be made from a list from the district societies. We are adding to the By-Laws, and we do not change the Constitution or the method by which the Councillors are elected. If the House of Delegates should refuse to elect a member whose name was submitted by the district society, they could do so, and it would then be up to the District Society to submit another name. This does not usurp the rights and privileges of the House of Delegates. The candidate, as submitted, would have to be voted upon by the district society.

Reference Committee to Consider the Reports of the Delegate to the AMA Medical Center Advisory Council, and Committee on Medical Education

Dr. Burt, chairman of this committee, presented the following reports and their discussions, which were adopted section by section and as a whole.

1. Report of the Delegate to the AMA. The report was reviewed by the committee who felt that it should be accepted in its entirety, with the exception of the second paragraph. One member of the Reference Committee wished to go on record to the effect that the population explosion has not involved the State of North Dakota at the present time, and he felt that contraceptive measures should not be paid for out of tax funds. The committee also wished to affirm support for Dr. Willard Wright in his effort to become President-Elect of the American Medical Association. This portion of the report, as amended, was adopted.

2. Report of the Representative to the Medical Center Advisory Council. This report was reviewed and the Reference Committee noted with pleasure the developments in the Medical School at the University of N.D. and expressed hope that such progress could be continued. This portion of the report was adopted.

3. Report of the Committee on Medical Education. The Committee reviewed the report and felt that it should be accepted in its entirety. However, in private discussion concerning admission policies of the Medical School, the consensus was that quite a number of qualified North Dakota people were not applying to the Medical School in Grand Forks, largely because of inability to obtain admission blanks without a considerable amount of philosophical discussion. The Reference Committee agreed that if admission blanks are requested, they should be sent to anyone, any place, and that admission policies should be continued from that point. This portion of the report was adopted. Dr. Burt moved that the report be adopted as a whole. The motion was seconded by Dr. Hieb and carried.

DR. A. C. BURT, *Chairman*
DR. R. H. DELANO, *Vice-Chairman*
DR. GEORGE H. HILTS
DR. C. J. BAUMGARTNER
DR. E. O. HIEB

Reference Committee to Consider the Reports of the Standing Committees

Dr. Tudor, chairman of this committee, presented the following reports and their discussions, which were adopted section by section and as a whole. He acknowledged the contributions of the committee and also the help of Drs. Boerth and McLean, chairmen of two Standing Committees, for their assistance in the preparation of the report.

1. Report of the Committee on Legislation. The committee, in reviewing the report, emphasized that doctor-legislator liaison begin at the Fall Interim Meeting and that there be increased legislative activity by state and local societies through AMPAC and COMPACT. This portion of the report was adopted.

2. Report of the Committee on Necrology and Medical History. This report was reviewed and approved, with the suggestion that in order to preserve the historical aspects of medicine in North Dakota, a medical history be compiled. For this purpose, they further suggested

that a separate committee on medical history be established. This portion of the report was adopted.

3. Report of the Committee on Public Health. The committee reviewed the report and found it acceptable. A suggestion was made by the Reference Committee that a special committee be appointed to propose legislation concerning the medical aspects of driver limitation. This portion of the report was adopted.

4. Report of the Committee on Public Relations. The committee reviewed the report and recommended that at the time of the Medical Board examinations, an orientation period be held by the State Medical Association for all applicants for medical licenses. It was further suggested that attendance at these orientation periods be made compulsory. This portion of the report was adopted.

The proposed Code of Cooperation, adopted by the Committee on Public Relations, September 7, 1964, was approved with one change suggested—the first sentence to read: "A Code of Cooperation is hereby set forth as a guide to the physician and hospital in their relationship with the radio, TV and press, bearing in mind always the pressing obligation and responsibility of all doctors and hospital personnel in the welfare of the patient." After some discussion, this portion of the report was adopted.

5. Report of the Committee on Rural and School Health. This report was reviewed and there was also a verbal report from the Committee Chairman, Dr. McLean. The Reference Committee recommended that this committee be discontinued, in view of the fact that its functions have been taken over by other committees of the Medical Association, civic groups and voluntary health associations. This portion of the report was adopted.

DR. TUDOR: "The Resolution of the Association of Minnesota Internists to be presented at the 1965 Minnesota State Medical Association Convention, was reviewed. We approve of this Resolution and recommend that the Executive Secretary, Mr. Lyle Limond, forward the Resolution to the American Medical Association, and forward our approval to the Association of Minnesota Internists." This portion of the report was adopted.

6. Report of the Committee on Official Publication. This report was reviewed with the recommendation that this committee be discontinued, and that its duties be handled through the office of the Executive Secretary. This portion of the report was adopted. Dr. Tudor moved that the report be adopted as a whole. The motion was seconded by Dr. Hankins and carried.

DR. ROBERT B. TUDOR, *Chairman*
DR. R. E. HANKINS, *Vice-Chairman*
DR. WARREN R. JENSEN
DR. A. M. CAMERON
DR. KENNETH HELENBOLT
DR. R. J. ULMER

Reference Committee to Consider Reports of the Committee on Medical Economics, and the Governor's Health Planning Committee

1. Report of the Committee on Medical Economics. This report, including the Advisory Committee to Public Assistance division of the State Welfare Board, was reviewed. The Reference Committee commended the efforts of Mr. Les Ovre of the North Dakota Welfare Board and Dr. R. W. Henderson, the medical advisor, for their efforts in bringing to the District Medical Societies the problems involved in providing medical aid to the needy of our state, and recommended that this policy be continued. It was the belief of the Reference Committee that through the use of the California Relative Value Schedule of 1964, the Committee on Medical Economics during the next year be urged to up-date the present Relative Value Schedule for North Dakota. This portion of the report was adopted.

The Reference Committee received a report from Dr. Ulmer, present Chairman of COMPACT in North Dakota, and noted with interest the remarks made before the House of Delegates by Dr. Henningsgaard of Oregon, Representative of AMPAC. Dr. Ulmer submitted three motions, which the Reference Committee recommended for favorable acceptance.

Motion 1. That each district medical society treasurer be requested to have AMPAC and COMPACT dues included with their annual billing and remit such dues to the Treasurer of COMPACT.

During the discussion that followed, Speaker Christoferson pointed out that for income tax purposes individual checks should be issued, as AMPAC and COMPACT dues are not deductible. Motion passed.

Motion 2. That the Chairman of the Council, with the approval of the Executive Committee of the Council, appoint the members of the COMPACT board annually. Dr. Ulmer moved for an amendment to this motion, changing it to read "the Chairman of the Council with the approval of the Councillors, appoint the board members of COMPACT," rather than the Executive Committee of the Council. This motion passed as amended.

Motion 3. That the Council be empowered to allocate funds or services for educational purposes through the Legislative Committee for COMPACT.

During the considerable discussion that followed, Dr. Giltner advised the members that a motion is not needed for the allocation of funds to the Legislative Committee by the Council. Dr. Mahowald pointed out that in the past, the Council has not earmarked a given amount of money for a specific purpose. Speaker Christoferson asked for a vote on this motion. Ayes, 12; opposed, 20. This motion did not carry.

Dr. Vinje announced that the Reference Committee had been requested to present a resolution regarding Social Security for physicians. He added that this resolution had been referred to the Resolutions Committee for action.

2. Report of the Governor's Health Planning Committee. This report was reviewed and the Reference Committee expressed its approval of the present disposition of available funds. Special note was taken of the fact that in anticipation of new funds for the renovation of hospitals during the coming year, the work of this Committee will be of greater importance. This portion of the report was adopted.

Dr. Vinje thanked all of the members of the Reference Committee for their participation, and also thanked the physicians who had appeared before this committee. The motion that the report as a whole be adopted was made by Dr. Vinje, seconded by Dr. Norum and carried.

DR. E. G. VINJE, *Chairman*
DR. H. A. NORUM, *Vice-Chairman*
DR. C. G. JOHNSON
DR. J. A. SANDMEYER
DR. RICHARD S. LARSON
DR. DONALD E. SKJEI

REPORT OF THE REFERENCE COMMITTEE ON RESOLUTIONS

Dr. Painter, chairman of the committee submitted the following resolutions:

RESOLUTION No. 1

Whereas, the members of the North Dakota State Medical Association, attending the Seventy-eighth Annual meeting of this

Association in Grand Forks, have enjoyed the hospitality and consideration of this great city, and,

Whereas, the Mayor of Grand Forks and his associates, the press, radio, hotels, and businessmen have contributed to make this session a memorable one,

Now, therefore, be it resolved that the House of Delegates express its appreciation by directing a copy of this Resolution to the Honorable Mayor of Grand Forks.

This resolution was adopted.

RESOLUTION No. 2

Whereas, the members of the North Dakota State Medical Association anticipate the increase in scientific knowledge to be gained from attendance at various exhibits, and

Whereas, the Exhibitors have shown unusual effort and ingenuity in developing their exhibits and thereby adding to the scientific interest at this meeting,

Now, therefore, be it resolved that the North Dakota State Medical Association extend to these Exhibitors our hearty welcome and thanks, and

Be it further resolved that a copy of this Resolution be forwarded to each Exhibitor.

This resolution was adopted.

RESOLUTION No. 3

Whereas, Dr. G. A. Dodds, President of the North Dakota State Medical Association for the year 1964-1965, did, in the years prior to his term of office, and in the year 1963-1964, as President-Elect of this Association, show an intense interest and devotion to the affairs and interests of the Association, and

Whereas, with the aid of his experience, knowledge, and concern relative to the practice of medicine in North Dakota, and with his dedication to the fulfillment of his office, Dr. Dodds did, in such an exemplary manner, lead this Association through the past year,

Now, therefore, be it resolved that the assembled delegates show their appreciation by a rising vote of thanks.

A rising vote of thanks adopted this resolution.

RESOLUTION No. 4

Whereas, the members of the North Dakota State Medical Association, attending the Seventy-eighth Annual Meeting have thoroughly enjoyed and profited by an excellent scientific program, and

Whereas, the host, the Third District Medical Society, and the various chairmen and committeemen have excelled in providing the members of the Association with the graciousness of a fine convention,

Now, therefore, be it resolved that the assembled delegates demonstrate their appreciation by a rising vote of thanks.

A rising vote of thanks adopted this resolution.

RESOLUTION No. 5

Whereas, the ladies of the Woman's Auxiliary to the North Dakota State Medical Association, through devoted enthusiasm and continuous efforts over the years have contributed diligently to the Medical Auxiliary Student Loan Fund of the Medical School of the University of North Dakota, and more recently to the American Medical Association Education and Research Foundation, and

Whereas, these funds have enabled many medical students to complete their medical education, and

Whereas, the local Auxiliary Societies throughout the State have participated in many other commendable projects which reflect credit to their organization and to the Medical Profession,

Now, therefore, be it resolved that the House of Delegates of the North Dakota State Medical Association convey to the Woman's Auxiliary our appreciation and thanks for their excellent work, and

Be it further resolved that a copy of this Resolution be directed to Mrs. Clyde L. Smith, and her successod.

This resolution was adopted.

RESOLUTION No. 6

Whereas, Mr. Lyle Limond, Mr. Dan Buchanan, and the Executive Secretary's staff have served the State Medical Association with diligence and proficiency during the immediate past year, as they have in preceding years,

Now, therefore, be it resolved that this House of Delegates formally show its appreciation with the adoption of this Resolution.

This resolution was adopted.

RESOLUTION No. 7

Whereas, the Legislature is considering in future years giving osteopaths full practice privileges in the State of North Dakota, and

Whereas, the medical profession recognizes that osteopathic schools have improved the standards of training and instruction in the scientific field in the past decade, and encourages further such improvement, and

Whereas, this Association feels that doctors of medicine in the best interest of the people of the state of North Dakota in obtaining medical care of the highest quality, should be instrumental in overseeing the medical care in this state,

Now, therefore, be it resolved that the House of Delegates favor consideration in the future of a composite board of medical examiners made up of members of medicine and osteopathy, proportionate to now existing MD-DO population, providing adequate study by the interested parties has been carried out, referred back to the House at its next meeting, and final approval of the House of Delegates delayed until the proposed written bill can be reviewed.

This resolution was adopted.

RESOLUTION No. 8

Whereas, the existing code regarding termination of pregnancy, which reads as follows, is unduly restrictive,

12-25-01. Procuring an abortion—Punishment—Every person who administers to any pregnant woman, or who prescribes for any such woman, or who advises or procures any such woman to take any medicine, drug or substance, or uses or employs, or procures or advises the use of any instrument or other means whatever, with intent thereby to procure the miscarriage of such woman, unless the same is necessary to preserve her life, shall be punished by imprisonment in the penitentiary for not less than one year nor more than three years, or in a county jail for not more than one year.

Whereas, certain instances of pregnancy should be terminated which do not threaten the life of the mother, such as pregnancy resulting from rape or incest,

Now, therefore, be it resolved that the North Dakota State Medical Association recommend that Section 12-25-01 be amended, by adding the following:

A licensed physician is justified in terminating a pregnancy if:

(a) He believes that there is substantial risk that continuance of the pregnancy would gravely impair the physical or mental health of the mother or that the child would be born with some grave physical or mental defect, or the pregnancy resulted from rape . . . or from incest; and

(b) Two physicians, one of whom may be the person performing the abortion, have certified in writing their belief in the justifying circumstances, and have filed such certificates prior to the abortion in the licensed hospital where it was to be performed, or in such other place as may be designated by law.

After discussion, the Chair entertained a substitute motion for referral of this Resolution to the Committee on Maternal and Child Welfare to be reintroduced for study and action at the next meeting. Dr. Jenson so moved, with the suggestion that there be more than two doctors certifying their belief in justifying circumstances. This motion passed.

RESOLUTION No. 9

Whereas, the North Dakota State Medical Association strongly supports a Tetanus Immunization Program as proposed by the American College of Surgeons and approved by the Council of the North Dakota State Medical Association, said program consisting of a Tetanus Immunization Week during which people would be urged to go to their doctors to be immunized,

Now, therefore, be it resolved that the House of Delegates go on record as approving such a program and to cooperate in its implementation.

This resolution was adopted.

RESOLUTION No. 10

Whereas, the majority opinion of the membership of the American Medical Association in the past has been opposed to including doctors of medicine under Social Security, and

Whereas, nothing has transpired which we believe would change this stand,

Now, therefore, be it resolved that the North Dakota State Medical Association, through its House of Delegates, go on record as still opposed to the inclusion of the Medical Profession under Social Security.

This resolution was adopted.

RESOLUTION No. 11

Whereas, the North Dakota State Medical Association provided an emergency room at the State Capitol during the 1963 and 1965 sessions of the Legislature; and,

Whereas, the emergency service at the Capitol required a physician in attendance each legislative day; and,

Whereas, the selection of physicians was done on a random

basis, with resulting confusion to the State's physicians and those responsible for filling the date,

Now, therefore, be it resolved that the Second District Medical Society is on record in requesting the North Dakota State Medical Association to establish a definite system for staffing the emergency room at the State Capitol during Legislative Assemblies; and,

Be it further resolved that the staffing be allocated proportionately to each District Society, to determine its own coverage accordingly.

This resolution was adopted.

RESOLUTION No. 12

Whereas, your Resolutions Committee has reviewed the Tennessee Medical Association Resolution referring to proposed federal programs, and possible impact of same on existing medical care in the United States; and

Whereas, such Resolution recommends that the American Medical Association vigorously study such proposals, cooperate in further discussion of same during the entire period of development and later legislative implementation, and further instructs the Tennessee Delegate to the American Medical Association to introduce an appropriate resolution in the House of Delegates of the American Medical Association,

Now, therefore, be it resolved that the House of Delegates of the North Dakota State Medical Association approve of such a resolution, and

Be it further resolved that the North Dakota State Medical Association's Delegate to the American Medical Association be instructed to support such a Resolution.

This resolution was adopted.

RESOLUTION No. 13

Whereas, Chapter IV, Section II of the By-Laws reads as follows:

"Each Component Society shall be entitled to send to the House of Delegates each year, 1 delegate for each 15 members and 1 for each major fraction thereof, but each district society holding a charter from this Association, which has made its annual report and paid its assessments as provided in this Constitution and By-Laws, shall be entitled to 1 delegate. In case a regularly elected delegate or alternate is unable to attend the annual meeting of the Association, the Speaker of the House of Delegates may appoint a substitute from the local society who shall have the rights and privileges of the regular delegates. Alternates may be seated in the House of Delegates, but shall not be entitled to vote if the delegate for whom they are an alternate is present."

Whereas, Section II has created a problem of uncertainty as to the number of delegates to be seated at the time of local society elections,

Be it therefore resolved, an addendum to Section II, Chapter IV, read as follows:

"The number of delegates to be seated in the House of Delegates will be determined by the number of paid-up members as of December 31st, of the previous year."

Be it further resolved that this proposed revision of the By-Laws be referred to the Committee on Constitution and By-Laws for its study and recommendation, and

Be it further resolved the House of Delegates make a decision of action at this session of 1965 to be incorporated on second reading in 1966, according to the Constitution and By-Laws.

A motion was made by Dr. Painter that this Resolution be referred to the Committee on Constitution and By-Laws. This motion was seconded and carried.

RESOLUTION No. 14

Whereas, in the past there have been resolutions introduced in the House of Delegates of which the members have little or no foreknowledge, and

Whereas, delegates have been forced to act on numerous resolutions, without knowing the feelings of their constituent chapter members,

Now, therefore, be it resolved that all resolutions be submitted in writing, in proper form, to the Speaker of the House, no later than two months prior to the Annual Meeting of the House of Delegates; or be submitted as a delayed bill which would require two-thirds majority vote to be considered at such Annual Meeting.

This resolution was not adopted.

RESOLUTION No. 15

Whereas, the purpose of a district delegate to the House of Delegates is to represent each individual district and receive instructions from the District Society, and

Whereas, the introduction of resolutions to the House of Delegates at a late date precludes the possibility of pre-examination of such resolutions,

Now, therefore, be it resolved that all resolutions to the House of Delegates must be submitted by March 1st of each year, and that late resolutions to the House of Delegates may be submitted for decision on a two-thirds vote of the House of Delegates.

This resolution was not adopted.

Dr. Painter thanked the members of the Reference Committee on Resolutions for their long and diligent work. He expressed hope that in the future more formal reference committee meetings could be held. He also asked that more members appear before the reference committee in support of, or opposition to, the various items of business.

Dr. Painter moved that the report as a whole be adopted. The motion was seconded by Dr. Dahl and carried.

DR. R. C. PAINTER, *Chairman*
DR. J. N. ELSWORTH, *Vice-Chairman*
DR. L. A. GILTNER
DR. P. O. DAHL
DR. W. C. HANEWALD
DR. PAUL J. BEITHON

At this time, Dr. Skjei moved that it be recommended that the Executive Secretary publish the proceedings of the Annual Meeting prior to the October issue of THE JOURNAL-LANCET so that the District Societies can have these proceedings before the fall meeting. This motion was seconded by Dr. Helenbolt and passed.

The treasurer's report was presented by Dr. Nierling as follows:

DR. NIERLING: You will find a summary of our financial condition on pages 28 to 32 in the Handbook. The budget for this year is $47,840.00. We feel we can stay within that amount as Lyle Limond is watching the expenditures of the funds. In last year's budget there were eighteen items and out of the eighteen, there were fifteen of them that were not entirely spent, three turned out on the debit side so the budget was not over extended last year. We have collected this year some $45,000.00 in dues. We have a little interest from funds invested. We feel that we will get some dues in that have not been paid as yet. There is still the problem of collecting dues. I am sure this is not too much of a problem so that we will get the others. It is the feeling of the Council and the Treasurer that the dues for next year should remain the same as the previous several years, of $100.00. If there is a deficit in this year's budget, next year you will hear from us. At our Convention in Minot we had a surplus of $300.00 because we now charge for the Mixer. The Conventions, therefore, are now pretty well self-supporting. If there are any questions or problems, I would be glad to answer them.

A move was made by Dr. Beithon, seconded by Dr. Painter, that the dues remain the same. Motion passed.

As there was no member of the North Dakota State Board of Medical Examiners present, Speaker Christoferson asked for a motion that a report from the Medical Examining Board be accepted as submitted and published in THE JOURNAL-LANCET. It was so moved by Dr. Dahl and seconded by Dr. Tudor. Motion passed.

The Speaker acknowledged the invitation from Dr. Burt that the Association hold the 1966 annual meeting in Fargo. Dr. Christoferson explained that this annual session would be held for three consecutive days, commencing on the Friday immediately preceding the first Sunday in May. He then entertained a motion for the meeting to be held in 1967. Dr. Nierling stated that in view of the limited facilities at Jamestown, the Seventh District had refrained from inviting the association to meet there. However, he added, it was the consensus of the members of the Seventh District Society that the meeting could be handled satisfactorily in 1967.

Dr. Tudor moved that the invitation to meet in Jamestown be accepted. The motion was seconded by Dr. Hanewald and carried.

Speaker Christoferson delegated the Council to compose the outline of the program to be held in Fargo in 1966, as directed in Chapter 5, and to notify the committees within the following three months as to the composition of the meeting.

The following is the report of the Nominating Committee. The slate of nominees, as presented by the Nominating Committee, was voted on singly as follows:

President ..... J. D. Craven, Williston
President-Elect ..... G. W. Toomey, Devils Lake
First Vice-President ..... V. J. Fischer, Minot
Second Vice-President ..... C. H. Peters, Bismarck
Secretary ..... W. M. Buckingham, Bismarck
Treasurer ..... R. D. Nierling, Jamestown
Delegate to the AMA ..... T. E. Pederson, Jamestown
Alternate Delegate to the AMA ..... R. C. Painter, Grand Forks
Speaker of the House of Delegates ..... Lee Christoferson, Fargo
Vice-Speaker of the House ..... P. O. Dahl, Bismarck

Nominated as councillors were Drs. DeCesare, First District; R. E. Mahowald, Third District; R. B. Tudor, Sixth District.

There were no additional nominations.

BOARD OF MEDICAL EXAMINERS

The following 2 names were to be submitted to the governor for the 3 physicians whose terms expire in 1965: J. W. Cleary, Bismarck; A. C. Fortney, Fargo.

To complete the list of nine nominees for the Board of Medical Examiners to be submitted to the governor, Dr. Gilsdorf proposed the following names: Drs. Paul Beithon, Wahpeton; Robert Fawcett, Devils Lake; Keith Foster, Dickinson; A. R. Gilsdorf, Dickinson; Frank Hill, Grand Forks; R. W. Larson, Velva; and R. Nierling, Jamestown.

Dr. Hanewald moved that all of the nominees be elected by unanimous ballot. The motion was seconded by Dr. Norum and passed.

As two names should be offered to the governor for a post on the State Health Council, Dr. Little was nominated and Dr. Owens renominated to serve on that council. Dr. Moses moved that the nominees be elected. The motion was seconded by Dr. Dahl and passed.

At this time Speaker Christoferson conveyed his thanks to the Nominating Committee for their complete report and also thanked the members for their show of confidence in him by his reelection as Speaker of the House of Delegates for the current year. Dr. Christoferson expressed his gratitude to Lyle Limond and his capable staff for their valuable assistance during the past year.

There being no further business, it was moved by Dr. Painter and seconded by Dr. Powers that the meeting be adjourned. Adjournment was at 5:25 P.M.

SCIENTIFIC PROGRAM

Monday, May 3, 1965

ARMORY-AUDITORIUM—GRAND FORKS, N.D.

8:30 A.M.—Registration
9:30-10:30 A.M.—"The Cerebral Vascular Accident"—to be discussed from these viewpoints:
Internal Medicine—Mack V. Traynor, Jr., M.D., Fargo, N.D.
Neurology—R. Natarajan, M.D., Grand Forks.
Physical Medicine—Miland E. Knapp, M.D., Minneapolis.
Neurosurgery—Gerd Fischer, M.D., Bismarck.
10:30-11:00 A.M.—Intermission
11:00 A.M.—Welcome from Mr. Hugo Magnuson, Mayor of Grand Forks, and from Dr. Kenneth S. Helenbolt, President, Grand Forks District Medical Society.
"The Cerebral Vascular Accident"—Second portion of program.
General Surgery—G. R. Swafford, M.D., Jamestown.
Orthopedic Surgery—J. J. McLeod, M.D., Grand Forks.
Psychiatry—Russell O. Saxvik, M.D., Bismarck.

NOON RECESS

2:00-2:30 P.M.—"Gynecology as Encountered in the Office"—Ralph A. Reis, M.D., Chicago, Ill.
2:30-3:00 P.M.—"Eye Signs in Systemic Disease"—William C. Frayer, M.D., Philadelphia, Pa.
3:00-3:45 P.M.—Intermission
3:45-4:15 P.M.—"Chromosomes in Human Disease"—W. A. Wasdahl, M.D., UND, Grand Forks.
4:15-5:00 P.M.—"The Current Treatment of Diabetes"—E. A. Haunz, M.D., Grand Forks.

Tuesday, May 4, 1965

ARMORY-AUDITORIUM—GRAND FORKS, N.D.

8:30 A.M.—Registration
9:30-10:00 A.M.—"Results of Brain Scanning with Radioactive Isotopes, and Correlations with Other Diagnostic Studies"—Mark H. Lane, M.D., Fargo.
10:00-10:30 A.M.—"Open (Retropubic) Prostatectomy and Simultaneous Preperitoneal Hernial Repair"—Leander W. Riba, M.D., Chicago, Ill.
10:30-11:15 A.M.—Intermission
11:15-11:35 A.M.—"Management, Referral, and Aftercare of the Mentally Ill by the Family Physician"—Marvin J. Geib, M.D., Fargo.
11:35-12:00 NOON—"Medications and the Active Treatment of Psychiatric Illnesses"—Theodore Larson, M.D., Minneapolis.

NOON RECESS

2:00-2:45 P.M.—"Some Psychosomatic Manifestations and Their Importance in Medicine"—G. S. Varnam, M.D., Winnipeg.
2:45-3:20 P.M.—"Disability Decision-Making Theory"—W. M. Roemmich, M.D., Baltimore.
3:20-4:00 P.M.—"Responsibility of the Private Physician for the Federal Vocational Rehabilitation Program"—Stanley S. Peterson, M.D., Springfield, Ill.

North Dakota State Medical Association Roster—1965

MEMBERSHIPS BY DISTRICTS

First District

Amidon, Blaine F. ..... Dakota Clinic, Fargo
Armstrong, William B. ..... Fargo
Bacheller, Stephen C. ..... Enderlin
Bakke, Hans ..... Lisbon
Barnard, Donald M. ..... Fargo Clinic, Fargo
Beithon, Elmer J. .. Red River Valley Clinic, Wahpeton
Beithon, Paul J. ... Red River Valley Clinic, Wahpeton
Beithon, R. Bruce ..... Fairmount Clinic, Fairmount
Beltz, Melvin E. ..... Wahpeton Clinic, Wahpeton
Bjerke, Leon A. .... Red River Valley Clinic, Wahpeton
Borland, Verl G. ..... Fargo Clinic, Fargo
Burt, Arthur C. ..... 308 Medical Arts Building, Fargo
Bushell, Robert P. ..... Fargo Clinic, Fargo
Christoferson, Lee A. ..... 700 1st Avenue S., Fargo
Christu, Chris M. ..... Fargo Clinic, Fargo
Crim, Eleanor M. ..... 405 17th Ave. S., Fargo
Darrow, Kent E. ..... Dakota Clinic, Fargo

DeCesare, F. A. ..... Dakota Clinic, Fargo
Dillard, James R. .... 208 Medical Arts Building, Fargo
Dodds, G. Alfred ..... Fargo Clinic, Fargo
Donat, T. L. ..... 408 Medical Arts Building, Fargo
Ehlen, Matt J. ..... Fargo Clinic, Fargo
Engstrom, Perry H. . . Red River Valley Clinic, Wahpeton
Fercho, Calvin K. .... 304 Medical Arts Building, Fargo
Fortney, Arthur C. ..... Fargo Clinic, Fargo
Gaebe, Robert C. ..... 700 1st Avenue S., Fargo
Geib, Marvin J. ..... 700 1st Avenue S., Fargo
Geston, Robert L. .... 402 Sheyenne Street, West Fargo
Gillam, John S. ..... Fargo Clinic, Fargo
Goff, John R. ..... Fargo Clinic, Fargo
Goltz, Neill F. ..... Fargo Clinic, Fargo
Gustafson, Maynard B. ..... 700 1st Avenue S., Fargo
Hall, G. Howard ..... Fargo Clinic, Fargo
Hamilton, Thomas M. ..... Fargo Clinic, Fargo
Hawn, Hugh W. ..... 624 Gate City Building, Fargo
Haynes, George H. ..... Lisbon
Heilman, Charles O. ..... Fargo Clinic, Fargo
Houghton, James F. ..... Dakota Clinic, Fargo
Hunter, C. M. ..... Medical Arts Building, Fargo
Hunter, G. Wilson ..... Fargo Clinic, Fargo
Irvine, Vincent S. ..... Lidgerwood
Ivers, George U. .... 424 deLendrecie Building, Fargo
Ivers, Robert R. ..... 700 1st Avenue S., Fargo
Jaehning, David G. ..... Hotel Wahpeton, Wahpeton
Jordheim, Robert ..... Fargo Clinic, Fargo
Kana, Dale C. ..... Medical Arts Building, Fargo
Kelly, William A. ..... Medical Arts Building, Fargo
Kohlmeyer, Albert C. ..... 700 1st Avenue S., Fargo
Kulland, Roy E. .... 402 Sheyenne Street, West Fargo
Lamb, Donald L. .... 204 Medical Arts Building, Fargo
Lancaster, W. E. G. ..... Fargo Clinic, Fargo
Landa, Marshall ..... Dakota Clinic, Fargo
Lane, Mark H. ..... 700 1st Avenue S., Fargo
Larson, G. Arthur ..... 1538 9th St. S., Fargo
Lawrence Donald H. .. 202 Medical Arts Building, Fargo
LeBien, Wayne E. ..... Fargo Clinic, Fargo
LeMar, John D. ..... Fargo Clinic, Fargo
Levine, Leonard ..... Fargo Clinic, Fargo
Lewis, A. K. ..... Lisbon
Lewis, T. H. ..... 302 Black Building, Fargo
Lindsay, Douglas T. ..... Fargo Clinic, Fargo
Lytle, Francis T. ..... Fargo Clinic, Fargo
McMahon, John M. ..... Dakota Clinic, Fargo
Macaulay, Warren L. ..... Fargo Clinic, Fargo
Magill, Gordon B. ... 400 Medical Arts Building, Fargo
Magness, John L. ..... Dakota Clinic, Fargo
Mazur, B. A. ..... Dakota Clinic, Fargo
Melton, Frank M. ..... Dakota Clinic, Fargo
Miller, Herbert H. ... 509½ Dakota Avenue, Wahpeton
Miller, J. W. ..... Dakota Clinic, Fargo
Murray, James B. ..... Dakota Clinic, Fargo
Nagle, Duane W. ..... Fargo Clinic, Fargo
Norum, Henry A. ..... Fargo Clinic, Fargo
Obert, Gerard J. ..... St. Luke's Hospital, Fargo
Ohrt, Harry A. ..... 408 Medical Arts Building, Fargo
O'Hearn, Jerome W. ..... Fargo Clinic, Fargo
Olin, Ronald ..... Fargo Clinic, Fargo
Oliver, James ..... Dakota Clinic, Fargo
Owens, Walter L. ..... Dakota Clinic, Fargo
Palmer, Wesley J. ..... Lisbon
Poindexter, Marlin H., Jr. ..... Fargo Clinic, Fargo
Poole, Ernest E. ..... Lidgerwood
Pray, Laurence G. ..... Fargo Clinic, Fargo
Rogers, Robert G. ..... Dakota Clinic, Fargo
Schleinitz, Fritz B. ..... Hankinson
Schneider, Joseph F. .... Medical Arts Building, Fargo
Sedlak, Oliver A. ..... 109 Roberts Street, Fargo
Seifert, Richard H. .. 402 Medical Arts Building, Fargo
Sessums, John V., Jr. ..... Dakota Clinic, Fargo
Shook, Lester D. ..... Fargo Clinic, Fargo
Spier, J. J. ..... 1720 S. University, Fargo
Stafne, William A. ..... Fargo Clinic, Fargo
Story, Robert D. ..... Fargo Clinic, Fargo
Swanson, Joel C. ..... 407 Black Building, Fargo
Thompson, George R. ..... Fargo Clinic, Fargo
Thorfinnson, Hugh D. ... Medical Arts Building, Fargo
Traynor, Mack V. ..... Fargo Clinic, Fargo
Triggs, Perry O. ..... Fargo Clinic, Fargo
Ulmer, Robert J. ..... Dakota Clinic, Fargo
Veitch, Abner ..... 502 Oak Street, Lisbon
Wall, Wendell H. ..... Wahpeton Clinic, Wahpeton
Wasemiller, E. R. ..... Wahpeton Clinic, Wahpeton
Webster, William O. ..... Fargo Clinic, Fargo
Weible, Earl B. ..... Abercrombie
Weible, Ralph D. ..... Dakota Clinic, Fargo
Wenz, E. P. ..... Dakota Clinic, Fargo
Wenzel, James B. ..... Dakota Clinic, Fargo
Weyers, Henry J. ..... 402 Sheyenne St., West Fargo
Williams, N. S. ..... Dakota Clinic, Fargo
Wiltse, Glenn L. ..... Wahpeton Clinic, Wahpeton
Wold, Lester E. ..... Fargo Clinic, Fargo

Second District

Cook, Stuart John ..... Rolette
Corbett, Conner A. ... Lake Region Clinic, Devils Lake
Coultrip, Raymond L., Jr. ..... McVille
Engesather, John A. D. ..... Lakota
Eylands, Jon V. ..... Rugby
Fawcett, John C. ..... Lake Region Clinic, Devils Lake
Fawcett, Robert M. ... Lake Region Clinic, Devils Lake
Fox, William R. ..... Johnson Clinic, Rugby
Gilbertson, Ernest V. .. Lake Region Clinic, Devils Lake
Glasner, Duane D. ..... Rolla
Gorrie, William A. ..... Maddock
Hillman, R. S. Lyle ..... Johnson Clinic, Rugby
Hilts, George H. ..... Cando
Johnson, Christian G. ..... Johnson Clinic, Rugby
Kihle, Kenneth W. ..... Bottineau
Klassen, Leonard .... 411 Fourth Avenue, Devils Lake
Lazareck, I. L. ..... 411 Fourth Avenue, Devils Lake
Lind, Jackson W. ..... Bottineau
Lund, A. B. ..... Leeds
McBane, Robert D. ... Lake Region Clinic, Devils Lake
McIntyre, Donald G. ..... Johnson Clinic, Rugby
Mahoney, James H. ... 411 Fourth Avenue, Devils Lake
Mari, Justo L. ..... Bottineau
Martin, George V. ..... Michigan Clinic, Michigan
Mattson, Clem J. ..... Palmer Clinic, Cando
Miller, C. Robert ..... 1207 Bennett, Bottineau
Neuenschwander, Allen R. ..... Rolla
Owens, Clarence G. ..... New Rockford
Pine, Louis F. ..... Lake Region Clinic, Devils Lake
Rinn, David A. ..... Cando
Sawchuk, John ..... Rolette
Schwinghamer, E. J. ..... New Rockford
Seibel, Glenn W. ..... New Rockford
Terlecki, J. ..... Minnewaukan
Toomey, Glenn W. .... Lake Region Clinic, Devils Lake
Towarnicky, Marvin J. ..... Fessenden
Turkula, William .... Lake Region Clinic, Devils Lake
Voglewede, William C. ..... Carrington
Wolf, Jerry D. ..... Bottineau

Third District

Barrie, James G. ..... Park River

Benson, T. Q. . . 1600 University Avenue, Grand Forks
Benwell, Harry D. . . . . Valley Medical Associates, Grand Forks
Bowes, H. Angus . . 1600 University Avenue, Grand Forks
Campbell, Duncan W. . Grand Forks Clinic, Grand Forks
Clark, Rodney . . . . . Grand Forks Clinic, Grand Forks
Clayburgh, Ben J. . . . . Grand Forks Clinic, Grand Forks
Cody, Gary D. . . . . LaMoure
Countryman, G. L. . . . . 1004 Hill Avenue, Grafton
Culmer, A. E., Jr. . . . . 501 1st National Bank Bldg., Grand Forks
Dailey, Walter C. . . . . Valley Medical Associates, Grand Forks
DeLano, Robert H. . . . . Northwood
Doss, R. Douglas . . 1600 University Avenue, Grand Forks
Eaton, L. P. . . . . Grafton Clinic, Grafton
Engelstad, O. D. . . . . University of N.D., Grand Forks
Evans, Harold W. . . . . Grand Forks Clinic, Grand Forks
Flaten, A. N. . . . . Edinburg
Glaspel, Cyril J. . . . . Grafton Clinic, Grafton
Goehl, R. O. . . . . Grand Forks Clinic, Grand Forks
Graham, C. M. . . 1600 University Avenue, Grand Forks
Graham, John H. Valley Medical Associates, Grand Forks
Grinnell, Ernest L. . . . Grand Forks Clinic, Grand Forks
Hardy, Nigel A. . . . . Minto
Harwood, T. H. . . . . University of N.D., Grand Forks
Haugen, C. O. . . . . Larimore
Haunz, Edgar A. . . . . Grand Forks Clinic, Grand Forks
Helenbolt, Kenneth S. . . . . 1600 University Avenue, Grand Forks
Helgason, Norman M. . . . . Cavalier
Helm, Richard K. . . . . Valley Medical Associates, Grand Forks
Hill, Frank A. . . . . Grand Forks Clinic, Grand Forks
Jensen, A. F. . . . . 1600 University Avenue, Grand Forks
Kaluzniak, N. . . . . Langdon
Keig, W. P., Jr. . . 1600 University Avenue, Grand Forks
Krahn, Henry . . . . . Walhalla
Lambie, John A. . . . . Grand Forks Clinic, Grand Forks
Landry, L. H. . . . . Walhalla
Larson, Eric J. . . . . Cavalier
Lee, Ya Pin . . . . . University of N.D., Grand Forks
Leigh, James A. . . 111 North Fifth Street, Grand Forks
Leigh, Ralph E. . . 111 North Fifth Street, Grand Forks
Leigh, Richard H. . . 1600 University Avenue, Grand Forks
Lorentson, Carl E. . . . Grand Forks Clinic, Grand Forks
McKay, John F. . . . . 703 S. 4th Street, Grand Forks
McLaughlin, Blaine E. . . University of N.D., Grand Forks
McLeod, John . . . . . Grand Forks Clinic, Grand Forks
Mahowald, Ralph E. . . 1400 Grand Avenue, Grand Forks
Mann, Hamish . . 1600 University Avenue, Grand Forks
Marshall, Robert A. . . . . 27 S. Third Street, Grand Forks
Meredith, William C. . . . . Drayton
Muus, J. M. . . . . McVille
Muus, O. Harold . . 27½ South Third Street, Grand Forks
Natarajan, R. . . . . 1600 University Avenue, Grand Forks
Nelson, Wallace W. . . Grand Forks Clinic, Grand Forks
Nelson, William C. . . Grand Forks Clinic, Grand Forks
Olson, James R. . . . . Grand Forks Clinic, Grand Forks
O'Toole, James K. . . . . 2707 Belle, Topeka, Kansas
Painter, Robert C. . . . Grand Forks Clinic, Grand Forks
Panek, A. F. . . . . Milton
Peake, Frances M. . . . . 14½ S. Third Street, Grand Forks
Penners, John H. . . . . Grand Forks Clinic, Grand Forks
Pettit, Samuel L. . . . . Grand Forks Clinic, Grand Forks
Piltingsrud, Harold R. . . . . Park River
Pinsonneault, W. A. . . . . Drayton
Porter, Charles B. . . . . Grand Forks Clinic, Grand Forks
Powers, William T. . . . . Valley Medical Associates, Grand Forks
Prochaska, Leonard J. . . . . 517 1st National Bldg., Grand Forks
Rand, Charles C. . . . . State School, Grafton
Ruud, John E. . . 1st National Bank Bldg., Grand Forks
Saiki, A. K. . . . . University of N.D., Grand Forks
Sande, C. W. . . . . Northwood
Sandmeyer, John A., . . Grand Forks Clinic, Grand Forks
Schafer, Thomas . . . . . Grand Forks Clinic, Grand Forks
Scheflo, Myron W. . . . . 1004 Hill Avenue, Grafton
Silverman, Louis B. . . Grand Forks Clinic, Grand Forks
Tarpley, Harold I. . . . . Valley Medical Associates, Grand Forks
Teevens, William P. . . . . Grafton Clinic, Grafton
Thorgrimsen, G. G. . . . . 1600 University Avenue, Grand Forks
Tompkins, C. R. . . . . 1004 Hill Avenue, Grafton
Vandergon, Keith G. . . 1400 Grand Avenue, Grand Forks
Wasdahl, Walter . . . . . University of N.D., Grand Forks
Webber, Freeman B. . . . . Harvey
Wilson, George A. . . . Grand Forks Clinic, Grand Forks
Woutat, Philip H. . . . . Grand Forks Clinic, Grand Forks
Youngs, Nelson A. . . . Grand Forks Clinic, Grand Forks

Fourth District

Amstutz, Kenneth N. . . . . Northwest Clinic, Minot
Ayash, John J. . . . . 123 2nd Avenue S.E., Minot
Barnes, James A. . . . . Medical Arts Clinic, Minot
Bermudez, E. . . . . Garrison Clinic, Garrison
Blatherwick, Robert . . . . . Parshall
Boyle, John T. . . . . Garrison Clinic, Garrison
Boyum, Lowell E. . . . . Harvey Medical Center, Harvey
Breslich, Paul J. . . . . Northwest Clinic, Minot
Briggs, Brian E. . . . . Main Medical Building, Minot
Cameron, Angus L. . . . . Northwest Clinic, Minot
Cameron, A. Malcolm . . . . . Northwest Clinic, Minot
Devine, John L., Jr. . . . . Great Plains Clinic, Minot
Dormont, Richard E. . . . . Northwest Clinic, Minot
Erenfeld, F. R. . . . . 617 N. Broadway, Minot
Fischer, V. J. . . . . Medical Arts Clinic, Minot
Flath, M. G. . . . . Stanley
Flickinger, Dale B. . . . . Medical Arts Clinic, Minot
Gammell, Robert T. . . . . Kenmare
Garrison, M. W. . . . . Garrison Building, Minot
Giltner, Lloyd A. . . . . Medical Arts Clinic, Minot
Goodman, Robert . . . . . Powers Lake
Gozum, Ekrem . . . . . 123 2nd Avenue S.E., Minot
Halliday, David J., Jr. . . . . Kenmare
Halverson, C. H. . . . . 401 S. Main, Minot
Hammargren, A. F. . . . . Harvey Medical Center, Harvey
Hart, George M. . . . . Northwest Clinic, Minot
Heidorn, G. H. . . . . Main Medical Building, Minot
Hoopes, Lorman L. . . . . 315 South Main, Minot
Hordinsky, B. Z. . . . . Drake
Huntley, Wellington B. . . . . 315 S. Main, Minot
Hurly, William C. . . . . Medical Arts Clinic, Minot
Huss, Bernard, Jr. . . . . Medical Arts Clinic, Minot
Jayapathy, B. . . . . 315 S. Main, Minot
Johnson, O. W. . . . . Johnson Clinic, Rugby
Keck, Stanley W. . . . . Northwest Clinic, Minot
Kermott, L. H., Jr. . . . . 401 Main Street S., Minot
Kohl, D. L. . . . . 123 2nd Avenue S.E., Minot
Lampert, M. T. . . . . 407 1st National Bank Bldg, Minot
La Rochelle, W. D. . . . . Stanley
Larson, Richard S. . . . . Velva
Leonard, Kenneth O. . . . . Garrison Clinic, Garrison
Leonard, Kermit . . . . . Garrison Clinic, Garrison
London, Carl B. . . . . Northwest Clinic, Minot
Matthaei, D. W. . . . . Fessenden
Naegeli, Frank D. . . . . Northwest Clinic, Minot

Nazli, Mehmet ..... 401 S. Main, Minot
Odegard, Russell L. ..... Great Plains Clinic, Minot
Olson, Burton G. ..... McCannel Clinic, Minot
Peterson, Myron D. ..... Medical Arts Clinic, Minot
Richardson, G. R. ..... Main Medical Building, Minot
Ringo, G. Roy ..... 119-A Main Street S., Minot
Rioux, B. ..... 14A S. Main, Minot
Rowe, Paul H. ..... Northwest Clinic, Minot
Sahl, Jens, Jr. ..... Northwest Clinic, Minot
Shea, Samuel E. ..... Main Medical Building, Minot
Sorenson, A. R. ..... Medical Arts Clinic, Minot
Sorenson, Roger ..... Medical Arts Clinic, Minot
Uthus, O. S. ..... 21½ 2nd Avenue S.E., Minot
Veenbaas, F. F. ..... Northwest Clinic, Minot
Wall, Willard W. ..... Northwest Clinic, Minot
Wallis, Marianne ..... Main Medical Building, Minot
Westervelt, A. E. ..... Bowdon
Wilson, Herbert J. ..... New Town

Fifth District

Berg, Milton O. ..... Valley City Clinic, Valley City
Carpenter, Eugene .. 130 Central Avenue S., Valley City
Christianson, Gunnar .... Valley City Clinic, Valley City
Feist, Donald J. ..... Forman
Goven, John W. ..... Valley City Clinic, Valley City
Jensen, Clayton E. ..... Valley City Clinic, Valley City
Jensen, Warren R. ..... 117 N.W. Third, Valley City
Klein, C. J. ..... Valley City Clinic, Valley City
Macdonald, A. C. .. 130 Central Avenue S., Valley City
Macdonald, Neil A. .. 130 Central Avenue S., Valley City

Sixth District

Amos, James R. .. Health Dept., Capitol Bldg., Bismarck
Anderson, F. E. ..... Underwood
Arneson, Charles ..... 405½ Broadway, Bismarck
Arnold, Helmut .... Quain & Ramstad Clinic, Bismarck
Baumgartner, C. J. .. Quain & Ramstad Clinic, Bismarck
Berg, H. Milton .... Quain & Ramstad Clinic, Bismarck
Berg, Roger M. .... Quain & Ramstad Clinic, Bismarck
Bertheau, H. J. ..... Linton
Boerth, E. H. .....
Workmen's Comp. Bureau, Capitol Bldg., Bismarck
Brink, Norvel O. .... Quain & Ramstad Clinic, Bismarck
Buckingham, T. W. ..... 405½ Broadway, Bismarck
Buckingham, William M. .. Capital City Clinic, Bismarck
Candy, Ardis Jean .. Quain & Ramstad Clinic, Bismarck
Carlsen, Donald A. ..... 104 2nd Ave. N.W., Mandan
Cartwright, John T. .. Missouri Valley Clinic, Bismarck
Cleary, Joseph W. .... Missouri Valley Clinic, Bismarck
Curiskis, A. A. ..... Elgin
Dahl, Phillip O. ..... Missouri Valley Clinic, Bismarck
Daniolos, D. P. .... Quain & Ramstad Clinic, Bismarck
Diven, Wilbur L. ..... 402½ Main, Bismarck
Dunnigan, Ralph J. ..... Capital City Clinic, Bismarck
Eriksen, Johan A. ..... St. Alexius Hospital, Bismarck
Ewert, Arthur O. ..... Beulah
Fardal, Richard W. ..Quain & Ramstad Clinic, Bismarck
Fischer, Gerhard .... Quain & Ramstad Clinic, Bismarck
Fischer, Hans ..... Quain & Ramstad Clinic, Bismarck
Fleck, Roland ..... Ashley
Fortman, Albert H., Jr. .. Capital City Clinic, Bismarck
Frankel, John B. .... Quain & Ramstad Clinic, Bismarck
Freise, Paul W. .... Quain & Ramstad Clinic, Bismarck
Fricke, Roger W. .. Quain & Ramstad Clinic, Bismarck
Gaebe, Otto C. ..... 1215 N. Mandan Street, Bismarck
Garrett, W. G. ..... Missouri Valley Clinic, Bismarck
Gibson, Thomas F. ..... Medical Arts Center, Mandan
Girard, B. A. ..... 107 First Ave. N.W., Mandan
Gonzalez, Gilberto .... Missouri Valley Clinic, Bismarck
Goodman, Edward ..... Napoleon
Goughnour, Myron W. .. Capital City Clinic, Bismarck
Gregware, Peter R. .. Quain & Ramstad Clinic, Bismarck
Griebenow, Frederick ..... 905 9th Street, Bismarck
Gutowski, Franz ..... Wishek
Hamilton, Charles A. Quain & Ramstad Clinic, Bismarck
Hanson, Harris D. .. Quain & Ramstad Clinic, Bismarck
Heffron, M. M. ..... 405½ Broadway, Bismarck
Henderson, Robert ..... Capital City Clinic, Bismarck
Hetzler, Arnold E. ..... 322 W. Main, Mandan
Hilts, Joseph A. ..... New Salem
Hook, William F. .. Quain & Ramstad Clinic, Bismarck
Icenogle, G. D. ..... State Hospital, Jamestown
Jacobson, M. S. ..... Elgin
Johnson, Kenneth J. .. Quain & Ramstad Clinic, Bismarck
Johnson, Marlin J. E. .. Quain & Ramstad Clinic, Bismarck
Johnson, Paul L. .... Quain & Ramstad Clinic, Bismarck
Kalnins, Arnold ..... Washburn
Kling, Robert R. .... Quain & Ramstad Clinic, Bismarck
Klosterman, Paul ..... Capital City Clinic, Bismarck
Knudsen, Jerry M. .... Missouri Valley Clinic, Bismarck
Kuplis, Haralds ..... Turtle Lake
Larson, Leonard W. .. Quain & Ramstad Clinic, Bismarck
Lindelow, O. V. ..... Missouri Valley Clinic, Bismarck
Lommen, Marwin A. K. .. Capital City Clinic, Bismarck
Lorenzen, F. C. ..... Carson
Milligan, Shelagh M. .... Medical Arts Center, Mandan
Montz, Charles R. .. Quain & Ramstad Clinic, Bismarck
Moreland, J. W. ..... 903 Crescent Lane, Bismarck
Moses, James J. .... Quain & Ramstad Clinic, Bismarck
Nuessle, Robert F. .. Quain & Ramstad Clinic, Bismarck
Null, William G. .... Quain & Ramstad Clinic, Bismarck
Oien, Dale R. ..... Quain & Ramstad Clinic, Bismarck
Orchard, Welland J. ..... Linton
Owens, Percy L. ..... Missouri Valley Clinic, Bismarck
Perrin, Edwin D. .. Quain & Ramstad Clinic, Bismarck
Peters, Clifford H. .. Quain & Ramstad Clinic, Bismarck
Peterson, Alice H. .....
State Health Dept., Capitol Bldg., Bismarck
Peterson, Earl D. ... Quain & Ramstad Clinic, Bismarck
Pfeifle, D. M. ..... Quain & Ramstad Clinic, Bismarck
Pierce, W. B. ..... 911 Ave. C. West, Bismarck
Pierson, R. Warren .. Box 66, Asmara, Eritrea, Ethiopia
Pitcher, Wayne H. .. Quain & Ramstad Clinic, Bismarck
Ralston, L. S. ..... Quain & Ramstad Clinic, Bismarck
Ramos, Pablo ..... Quain & Ramstad Clinic, Bismarck
Riecke, William C. .. Quain & Ramstad Clinic, Bismarck
Samuelson, A. F. ..... 405 Broadway, Bismarck
Sauer, John P. ..... Missouri Valley Clinic, Bismarck
Saxvik, Russell O. .. Quain & Ramstad Clinic, Bismarck
Schoregge, Robert D. .. Quain & Ramstad Clinic, Bismarck
Smeenk, H. Pieter .. Quain & Ramstad Clinic, Bismarck
Smith, Clyde L. ..... Missouri Valley Clinic, Bismarck
Spielman, George H. .. 710 Oakwood Drive, Anoka, Minn.
Tarnasky, Ralph E. ..... St. Alexius Hospital, Bismarck
Thakor, S. J. ..... 405 Broadway, Bismarck
Tolstedt, G. E. .... Quain & Ramstad Clinic, Bismarck
Tudor, Robert B. .. Quain & Ramstad Clinic, Bismarck
VanVranken, Arthur E. .....
Quain & Ramstad Clinic, Bismarck
Vinje, Edmund G. ..... Hazen Clinic, Hazen
Vinje, Ralph ..... 405 E. Broadway, Bismarck
Vonnegut, F. F. ..... Linton
Waldschmidt, William D. .....
Quain & Ramstad Clinic, Bismarck
Zukowsky, A. ..... Steele

Seventh District

Beall, John A. ..... Professional Bldg., Jamestown

Bishop, James R. E. . . . . Professional Bldg., Jamestown
Bolliger, Eugene F. . . . . Ellendale
Carbone, H. A. . . . . State Hospital, Jamestown
Clement, Duane . . . . . Professional Bldg., Jamestown
Craychee, W. A. . . . . Oakes
Cukurs, Paul . . . . . State Hospital, Jamestown
Curtis, Philip B. . . . . Medical Arts Clinic, Jamestown
Elsworth, J. N. . . . . DePuy-Sorkness Clinic, Jamestown
Engberg, Roger D. . . DePuy-Sorkness Clinic, Jamestown
Fergusson, V. D. . . . . Edgeley
Gronewald, T. W. . . . . State Hospital, Jamestown
Hieb, Edwin O. . . . . DePuy-Sorkness Clinic, Jamestown
Hill, Wayne Allen . . . . . Kulm
Hogan, Clifford W. . . DePuy-Sorkness Clinic, Jamestown
Jansonius, J. W. . . . . Medical Arts Clinic, Jamestown
Larson, Ernest J. . . . DePuy-Sorkness Clinic, Jamestown
Lucy, Robert E. . . . . DePuy-Sorkness Clinic, Jamestown
Melzer, Simon W. . . . . Woodworth
Martin, Clarence S. . . . . Medina
Miles, James V., Jr. . . . . 1209 5th Ave. S.E., Jamestown
Nierling, Richard D. . DePuy-Sorkness Clinic, Jamestown
Pederson, T. E. . . . . DePuy-Sorkness Clinic, Jamestown
Sakai, Masahiro . . . . DePuy-Sorkness Clinic, Jamestown
Sorkness, Joseph . . . . DePuy-Sorkness Clinic, Jamestown
Swafford, G. R. . . . . DePuy-Sorkness Clinic, Jamestown
Swenson, J. A. . . . . 6020 York Ave. S., Edina, Minn.
Turner, N. W . . . 885 Longview Rd., Hillsborough, Calif.
Van der Linde, J. M. . . Medical Arts Clinic, Jamestown
Van Houten, R. W. . . . . Oakes
Woodward, R. S. . . . DePuy-Sorkness Clinic, Jamestown

Eighth District

Borrud, Chester C. . . . . Harmon Park Clinic, Williston
Craven, John P. . . . . Craven-Hagan Clinic, Williston
Craven, Joseph D. . . . . Craven-Hagan Clinic, Williston
Ellis, Gordon E. . . . . Harmon Park Clinic, Williston
Fennell, William L. . . . . Crosby Clinic, Crosby
Hagan, Edward J. . . . . Craven-Hagan Clinic, Williston
Harvey, Eoin S. . . . . Tioga
Jamieson, John . . . . . Tioga
Johnson, Alan K. . . . . Williston Clinic, Williston
Jun, Chang Sik . . . . . Crosby Clinic, Crosby
Lund, Carroll M. . . . . Williston Clinic, Williston
McCoy, F. E. . . . . 107 E. 18th St., Williston
McPhail, Clayton O. . . . . Crosby Clinic, Crosby
Okeson, G. C. . . . . Craven-Hagan Clinic, Williston
Oliver, Donald C. . . . . Watford City
Olson, M. Jerome . . . . . Williston Clinic, Williston
Olson, Robert J. . . . . 1240 8th Ave. W., Williston
Skjei, Donald E. . . . . Williston Clinic, Williston
Strinden, Dean R. . . . . Harmon Park Clinic, Williston
Wiederanders, R. E. . . . Harmon Park Clinic, Williston
Wright, Willard A. . . . . Williston Clinic, Williston

Ninth District

Ahlness, Paul . . . . . Bowman
Bush, Clarence A. . . . . Beach
Carter, Robert G. . . . . Hettinger
Dukart, Ralph J. . . . . Dickinson Clinic, Dickinson
Foster, Keith G. . . . . Rodgers-Gumper Clinic, Dickinson
Gilliland, R. F. . . . . Dickinson Clinic, Dickinson
Gilsdorf, Amos R. . . . . Dickinson Clinic, Dickinson
Guloien, H. E. . . . . Dickinson Clinic, Dickinson
Gumper, Arnold J. . . Rodgers-Gumper Clinic, Dickinson
Hanewald, W. C. . . Rodgers-Gumper Clinic, Dickinson
Hankins, Robert E. . . . . Mott
Hill, S. W. . . . . Regent
Hlavinka, D. J. . . . . Mayville
Larsen, Harlan C. . . Rodgers-Gumper Clinic, Dickinson
Maercklien, O. C. . . . . Mott
Nicely, Donald A. . . Rodgers-Gumper Clinic, Dickinson
Ordahl, Norman B. . . Rodgers-Gumper Clinic, Dickinson
Raasch, Richard F. . . . . 30 W. 8th Street, Dickinson
Reichert, Donald J. . . . . 24 W. Villard, Dickinson
Reichert, H. Lawrence . . . . . 24 W. Villard, Dickinson
Retzer, Paul G. . . . . Hettinger
Sawchuk, A. C. . . . . Dickinson Clinic, Dickinson
Schumacher, W. A. . . . . 12102 Silver Fox Rd., Los Alamitos, Calif.
Skwarok, Walter S. . . . . Hebron
Slominski, H. . . . . Richardton
Smith, Oscar M. . . . . P.O. Box 1188, Dickinson
Spear, Albert E. . . . . 610 First Ave. W., Dickinson
Thom, Robert C. . . . . Bowman

Tenth District

Breen, Donald J. . . . . Hillsboro
Kloster, Ronald M. . . . . Mayville
La Fleur, H. A. . . . . Mayville
Leckie, Michael I. . . . . Cooperstown
Little, James M. . . . . Mayville
Little, Roy C. . . . . Mayville
McLean, Robert W. . . . . Hillsboro
Oja, Karl F. . . . . Portland
Wakefield, Kenneth M. . . . . Cooperstown

(To be Continued)

Book Reviews . . .

Educating Tomorrow's Doctors

by MILTON J. HOROWITZ, *264 pp., Appleton-Century-Crofts, New York City, 1964. $5.50*

The most extensive and widely discussed post-World War II experimental study in medical education has been that conducted in the early 1950s by the Western Reserve University School of Medicine. During and after the resultant change in medical curriculum at Western Reserve, an elaborate effort was made to study and evaluate the numerous complex forces and factors which bear on the medical student, the physician-teacher, and their medical school environment in molding the major product of medical education, the new physician. One important segment of that multifaceted study is reported in the volume by Milton J. Horowitz, "Educating Tomorrow's Doctors."

The book consists of 2 quite distinct sections plus an extensive appendix. The first and smaller portion, entitled "Approaches to the Student," recapitulates the evolution, philosophy, and format of the revised medical school curriculum at Western Reserve. This fascinating story of the development and fruition of an educational idea has been recounted previously in journal articles and national meetings. This is seen, for example, in Horwitz's reference list on page 33. Apparently this portion of the book was considered a necessary preamble to an understanding of the larger, more original, newly reported second section. The theme of approach undertaken by the author in this study is epitomized in the heading on page 9, which reads, "The Development of the Student as a Focus for Inquiry."

The major portion of the book reports in personalized, individual form "profiles" or case studies of 20 medical students swept up in the swirling currents of the new program in medical education as it developed at Western Reserve. Dr. Horowitz, an assistant professor of psychology in the department of psychiatry at that institution, and his colleagues attempted to probe the motivations, aspirations, personal achievements, disappointments, and individual triumphs of each subject as he progressed through the four years of "phases" and "subject committees" that form the organizational basis for the Western Reserve system of medical teaching. A major portion of the reported data was collected in a series of interviews conducted with each student at certain selected intervals in his four-year medical curriculum. Other information was obtained through faculty evaluations, annual comprehensive examinations, national board examinations, medical school records, and questionnaires.

The critical problem, of course, is the enigma which plagues all medical educators who sincerely desire to study scientifically the results of their efforts as they modify educational programs and teaching methods. A given student can receive a basic medical education only once in a given period and a given environment. Controlled, comparative, systematized experimentation and evaluation are a priori impossible to achieve in investigation of this dynamic, complex system.

Most student problems revealed in the profiles are those which constitute the daily fare of the medical school dean's office and faculty counselor. Tomorrow's doctors-in-training, like other human beings, are sensitive and reactive to the human forces which shape attitudes and responses. They are affected in their pursuit of medical knowledge and competence by numerous intramural factors, including fatigue, excessive factual material, busy teachers engrossed in their research specialties, strain of impending assignments and examinations, a disadvantageous position in the academic "pecking order," self-comparisons with their colleagues, and developing professional identification. The author emphasizes the challenge of increasingly greater responsibility, including the responsibility for educating himself, which confronts the medical student as he advances toward physicianhood.

All of these problems and factors—and more—are presented in the pages of "Educating Tomorrow's Doctors" as the 20 medical students' case reports unfold.

Every physician concerned with the total contribution of medicine to society is properly interested in the general patterns and plans of medical education. This volume, however, is addressed primarily to psychologists and full-time medical educators as an addition to the growing field of research in medical education. Dr. Horowitz has sharpened the focus on the complexity of the medical student and the medical educational process. He has reported extensively on one important aspect of medical education, the psychological "set" of the student in his environment. The book contributes to our realization and understanding of the medical student as an individually evolving professional person—tomorrow's doctor.

H. MEAD CAVERT, M.D.
Minneapolis

Biochemical Diseases: Chemical Pediatrics

by I. NEWTON KUGELMASS, M.D., *1,229 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $35.50*

The series, American Lectures in Living Chemistry, offers ". . . the newer knowledge of chemical medicine in the cause of clinical practice" with this mongraph covering the biochemistry of pediatrics. The name of Dr. I. N. Kugelmass assures the reader of factual authenticity. The approach is biochemical and presents the material from the chemical angle, emphasizing the basic causes and mechanisms as a support for management of the disorders.

The book is divided into 3 sections: part 1 covering the communicative system, part 2 the constitutional system, and part 3 the component sysstems. The usual biochemical abbreviations are used frequently throughout, but a list of their meanings is placed at the front of the book for easy reference.

In the section on the communicative system, intellectual, neurological, pituitary, thyroid, adrenal, pancreatic, testicular, ovarian, and intersex disorders are treated in detail, with full attention given to genetic causes and in-

(Continued on page 18A)



On Stelazine® brand of trifluoperazine she's calm and alert

When a tranquilizer is needed, 'Stelazine' can regulate the level of anxiety so that the patient is unlikely to overreact to stress but is not tranquilized into psychic inertia. Patients on 'Stelazine' often experience a sense of mental alertness and, because they feel so much better, are more interested in their normal activities.

Contraindicated in comatose or greatly depressed states due to CNS depressants and in cases of existing blood dyscrasias, bone marrow depression and pre-existing liver damage. *Principal side effects,* usually dose-related, may include mild skin reaction, dry mouth, insomnia, fatigue, drowsiness, dizziness and neuromuscular (extrapyramidal) reactions. Muscular weakness, anorexia, rash, lactation and blurred vision may also be observed. Blood dyscrasias and jaundice have been extremely rare. Use with caution in patients with impaired cardiovascular systems.

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"I can't cope any more...
I worry about everything.
I don't sleep well...
wake up tired and irritable."

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consider starting the patient on 'Deprol'

1. 'Deprol' can help lift the mood of the depressed patient.

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3. Patients often report and show noticeable improvement within a short period of time.

4. In seven years of clinical use, side effects with 'Deprol' at recommended dosage have been infrequent and usually easily controlled.

5. No incompatibility with other medications has been reported to date. However, the possibility of additive effects should be considered.

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Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

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(Continued from page 424)

born errors of metabolism. In the chapter on pancreatic disorders, the use of the various types of insulin is well covered, but only scant notice is given to oral control. The use of the sulfonylureas and phenethylbiguanide is now sufficiently well accepted clinically for more thorough treatment.

In the second section on the constitutional system, nutritional, organic metabolic, inorganic homeostatic, electrolyte, allergic, erythrocyte, hemoglobin, pigment, and leukemic disorders and collagenic and hemorrhagic diseases are covered. There is some overlapping, for example, in the functions of the vitamins, but in an arrangement like this it is unavoidable and not at all distracting. It is noteworthy that the use of antihistamines in allergic disorders is not even mentioned. The slower and less dependable but perhaps more permanent desensitization methods are discussed at length, but the only reference in the entire book to antihistamines is in the third section, where a paragraph on antihistaminic poisoning appears in the chapter on environmental disorders. Dr. Kugelmass may prefer not to use these compounds but their use is surely based on biochemistry and deserves recognition.

In the third section, digestive, liver, pulmonary, cardiac, kidney, bone, neuromuscular, surgical, and environmental disorders are presented. In the chapter on digestive disorders, a discussion of the microbiological flora of the intestinal tract is neglected. The recent work of Dubos and Schaedler at Rockefeller Institute has demonstrated its importance to the health of the organism as a whole, but this omission may be excused on the basis of its microbiological rather than biochemical nature.

Typographically, the book is excellent. It is printed in clear, readable type on sturdy bond paper. A good index adds greatly to its usefulness. Every chapter is followed by an ample bibliography, although there are few references later than 1960. Primarily, the book is a reference work and as such it will be of use to both student and busy practitioner.

DAVID B. SABINE
Yonkers, N.Y.

Business Management of a Medical Practice

by BERNARD D. HIRSH, LL.B., *190 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1964. $7.75*

In this presentation, Bernard Hirsh does a commendable job in presenting the administrative details of medical solo and group practice, as well as the doctor's personal affairs. In Mr. Hirsh's book the advantages and disadvantages of sharing office space with other doctors are explored. Partnership provisions are discussed, as well as the doctor buying on credit, and renting office space. Other problems that the doctor needs to consider in starting out and continuing in practice by himself or with other associates are also presented. The book should also prove invaluable to attorneys, accountants, and clinic managers who are functioning in an advisory capacity to doctors. As Mr. Hirsh has stated in the preface, the book is not intended as a complete treatise on all of the various aspects of solo or group practice but rather as a highlight to some of the more common considerations. The index provides a ready reference by subject matter as it applies to medical practice.

(Continued on page 20A)

when treatment might precipitate a problem with monilia

especially in diabetics or debilitated patients

and in patients with a history of fungal overgrowth—during pregnancy—patients on steroids who require antibiotics—the elderly. The antimonilial specificity of Nystatin plus the extra benefits of DECLOMYCIN Demethylchlortetracycline allow lower mg intake per dose per day, the option of b.i.d. dosage, higher activity levels, 1-2 days' "extra" activity.

Side Effects typical of tetracyclines include glossitis, stomatitis, proctitis, nausea, diarrhea, vaginitis, dermatitis, overgrowth of nonsusceptible organisms, tooth discoloration (if given during tooth formation) and increased intracranial pressure (in young infants). Also, very rarely, anaphylactoid reaction. Reduce dosage in impaired renal function. Because of reactions to artificial or natural sunlight (even from short exposure and at low dosage), patient should be warned to avoid direct exposure. Stop drug immediately at the first sign of adverse reaction. It should not be taken with high calcium drugs or food; and should not be taken less than one hour before, or two hours after meals.

Average Adult Daily Dosage: four divided doses of 1 capsule each or two divided doses of 2 capsules.

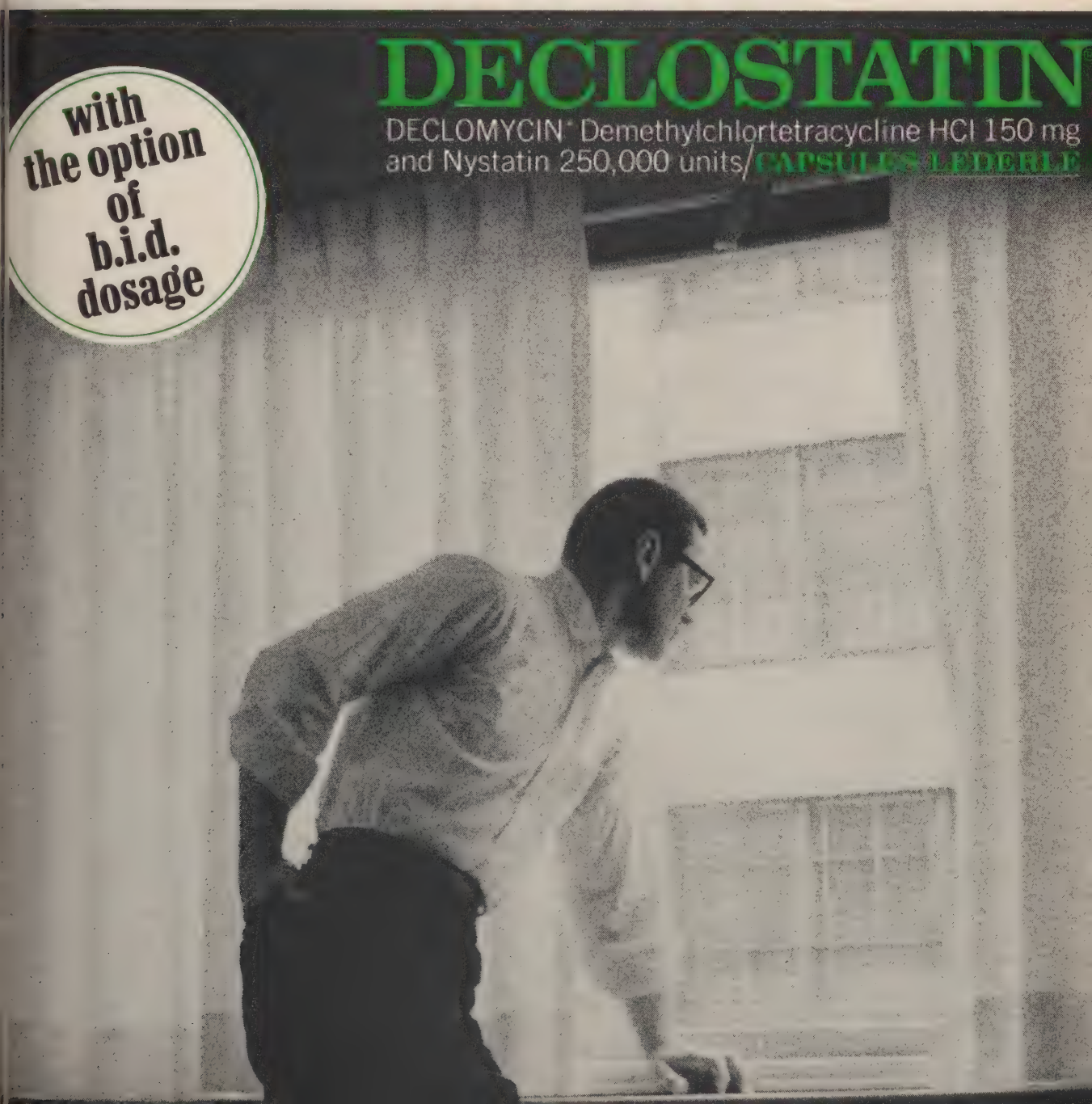
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(Continued from page 18A)

In the chapter on the "Partnership" many examples are included of various forms of possible partnership agreements. The author has drawn on partnership contracts made available to him and the examples represent one of the finest cross sections of agreements to be used as a check list with which this writer has been confronted. Other forms of legal documents are also presented that the doctor might have occasion to use. These documents are presented in a layman's language and are easily understood. They give the reader a good résumé of the pitfalls confronting a doctor who considers contracts regarding leases, the practice of medicine with associates, hospital relationships, financing a new car, and so forth.

The chapter dealing with "Wills, Trusts and Estates" became quite technical at times, but, also, shows the need for legal advice when complications set in or questions arise regarding one's personal estate. Sample wills are well illustrated in the text which shows various combinations for naming beneficiaries, revocations of the will, and so forth.

In reviewing the various aspects of "The Federal Income Tax," the author covers well the specifics of filing a return, deductible expenses, depreciation, and capital gains and losses. The reader is even informed as to what should be done if his return is examined by auditors. Again, illustrated completed tax forms and tables prove most helpful in giving a complete picture of our progressive income tax structure and in informing the reader what to watch for in filing his tax return.

Except for a few isolated sections, the book is easy to read and the material throughout is presented in a concise, straightforward manner. It should make a good reference book for the busy doctor.

DON DENNESON
Austin

NEW BOOKS RECEIVED

Two Centuries of Medicine by GEORGE W. CORNER, 363 pp., ill., J. B. Lippincott Co., Philadelphia, 1965. $7

Chelation Therapy by ALFRED SOFFER, MAYNARD CHENOWETH, GUNTHER L. EICHHORN, BETTY ROSOFF, MARTIN RUBIN, and HERTA SPENCER, 163 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $8

Annual Report of the Board of Regents of the Smithsonian Institution compiled by the SMITHSONIAN INSTITUTION, 595 pp., U.S. Government Printing Office, Washington, D.C., 1964. $4.25

Memory: A Contribution to Experimental Psychology by HERMANN EBBINGHAUS, 123 pp., ill., Dover Publications, New York City, 1964. $1.50

Diet and Bodily Constitution edited by G. E. W. WOLSTENHOLME and MAEVE O'CONNOR, 120 pp., ill., Little, Brown & Co., 1964. $2.95

Synopsis of Pathology by W. A. D. ANDERSON, 6th ed., 883 pp., ill., C. V. Mosby Co., St. Louis Mo., 1964. $9.75

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Dosage
Anturane, brand of sulfinpyrazone, is available as white, scored tablets of 100 mg. Initially, give half a tablet 4 times daily with meals or milk, increasing in one week to one tablet q.i.d. Increase to two tablets q.i.d. if necessary, and reduce if possible to as low as half a tablet q.i.d. after control. Continue through acute attacks, which can be concomitantly treated with phenylbutazone.

Patients on other uricosurics may be transferred to this drug at full dosage.

Contraindications
Active peptic ulcer. Salicylates and citrates antagonize the drug's action and are contraindicated for concomitant use.

Warning
Use with caution in pregnant women.

Precautions
Keep patients under close supervision and make periodic blood counts. Use cautiously in patients sensitive to pyrazoles, in patients with histories of peptic ulcer, and in conjunction with sulfa drugs, the sulfonylurea hypoglycemic agents, and insulin, the actions of which may be potentiated.

In mobilizing urate deposits, the drug may precipitate acute attacks of gout, urolithiasis, and renal colic, especially in the initial stages of therapy. Ensure adequate fluid intake and alkalinize the urine. With renal impairment, test renal function periodically.

Adverse Reactions
The most frequent are upper gastrointestinal disturbances. The drug may activate peptic ulcer. Rash occurs infrequently. Although not reported to date, blood dyscrasias are a possibility.

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in gout



Anturane®
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"the most effective and best tolerated of the currently available uricosuric agents for the control of gout."*

Anturane, brand of sulfinpyrazone, was developed in the Geigy laboratories. Its pharmacologic activity is limited almost exclusively to increasing the urinary excretion of uric acid. For this reason, it is a drug of choice in chronic tophaceous gout and acute intermittent gout. It is not intended for relief of acute attacks of gout.

In most patients, the drug rapidly reduces serum uric acid levels to normal. This not only prevents new tophi but also mobilizes and promotes the excretion of urates already in the tissues. The reduction of tophi and periarticular crystals results in more mobile, less painful joints.

Anturane, brand of sulfinpyrazone, materially reduces the number and severity of acute attacks of gout. It may also be used to counteract hyperuricemia induced by certain diuretics.

Because of its potency, the drug is often effective in patients refractory to other uricosuric agents. Patients can usually be maintained indefinitely on it without cumulative effects or development of tolerance.

Geigy

*Kuzell, W. C., et al.: Effect of sulfinpyrazone on serum uric acid in gout: a long-term study, Geriatrics 19:894, 1964.

News Briefs . . .

North Dakota

DRS. JOHN S. COLDIRON, ROBERT R. MOOSE, and FRANCIS BROWN have left the staff of the Public Health Service Indian Hospital at Belcourt to undertake residency programs. Dr. Coldiron will be replaced as service unit director by Dr. Walter Gower of the Indian Hospital staff.

* * * *

DR. JAMES R. DILLARD, who has practiced in Fargo for twenty-seven years, discontinued active practice in July. Dr. Dillard graduated from the University of Texas, Galveston, in 1924, and came to Fargo in 1938. He specialized in obstetrics and gynecology and is a member of the American Proctologic Society and the International College of Surgeons.

* * * *

DR. CECIL C. RAM, formerly of Aiken, S.C., has joined the urology staff of the Medical Arts Clinic, Minot. Dr. Ram graduated from the Medical College of South Carolina, Charleston, in 1954, and has been in private practice in Aiken since 1959.

* * * *

DR. ALBERT F. SAMUELSON, psychiatrist, has resigned as director of mental health services with the State Department of Health to go into private practice. Dr. Samuelson's new office will be in Bismarck.

* * * *

DR. JERRY M. KNUDSEN, surgeon at the Missouri Valley Clinic, Bismarck, has received certification as a diplomate of the American Board of Surgery. Dr. Knudsen received his medical degree from Baylor University, Houston, Texas, in 1956, and completed his residency in general surgery at Ancker Hospital, St. Paul.

* * * *

DR. ALBERT H. FORTMAN, surgeon at the Capital City Clinic, Bismarck, has been certified by the American Board of Surgery. Dr. Fortman received his M.D. degree from Northwestern University in 1954 and took a surgical residency at Cook County Hospital, Chicago, from 1954 to 1960. He is on the staff of St. Alexius, Bismarck, and Mandan Community Hospitals.

* * * *

DR. SEWARD K. IMES has joined the staff of the Quain and Ramstad Clinic, Bismarck, as head of the department of radiology. A native of Denver, Colo., Dr. Imes received his medical degree from the University of Nebraska in 1948. Since 1956 he has practiced radiology in the Denver area. Dr. Imes is a diplomate of the American Board of Radiology and a member of the American College of Radiology.

Minnesota

DR. NELS N. SONNESYN has been elected chief of the medical staff at the Minnesota Valley Memorial Hospital, Le Sueur. Dr. Sonnesyn, a general practitioner, has practiced in Le Sueur for about thirty years. He succeeds Dr. Dale A. Bergeron who has accepted an internal medicine residency at San Francisco.

DR. ROY E. DAUMANN, originally of Madison, has joined the staff of the Jackson Medical Center. Dr. Daumann received his medical degree from the University of Minnesota in 1964, and interned at Ancker Hospital, St. Paul.

* * * *

DRS. BENNIE C. FAUL and BRUCE W. WELLS have been appointed to the staff of the Worthington Clinic, Worthington. Dr. Faul, pediatrician, received his medical degree in 1961 from the University of North Dakota, Grand Forks, and Dr. Wells, general practitioner, from the University of Kansas, Kansas City, in 1964.

* * * *

DR. CHARLES W. QUIMBY, anesthesiologist, has joined the staff of the Community Memorial Hospital, Winona. Dr. Quimby received his medical degree from the University of Pennsylvania in 1954, and from 1960 to 1962 studied anesthesiology at the University of Minnesota Medical School.

* * * *

DR. ROBERT D. MATHISON of Minneapolis has moved to Annandale where he is associated in practice with Dr. Lester H. Bendix. Dr. Mathison graduated in 1963 from the University of Minnesota Medical School.

* * * *

DR. CECIL M. LEITCH, a general practitioner, has become a member of the Litchfield Clinic staff. Dr. Leitch graduated from the University of Washington School of Medicine, Seattle, in 1962, and completed his internship at Hennepin County General Hospital, Minneapolis. He recently was on the staff of the Public Health Service Hospital at Winslow, Ariz.

* * * *

DR. JOHN E. FINCH, pediatrician at the Mankato clinic, has been elected a fellow of the American Academy of Pediatrics. Dr. Finch is a 1959 graduate of the Washington University School of Medicine, St. Louis, Mo.

* * * *

DR. WILLIAM C. BERNSTEIN, clinical professor of surgery and director of the division of proctology, University of Minnesota, has been elected vice-president of the American Proctologic Society.

* * * *

DR. M. ALPHEUS BURNS, 92, of Milan, has been honored by his community in recognition of more than fifty years of service as a practicing physician. July 24 was set aside as "Dr. M. A. Burns Recognition Day." Dr. Burns still goes to his office every day. Associated with him in medical practice is his son, Dr. Floyd M. Burns.

* * * *

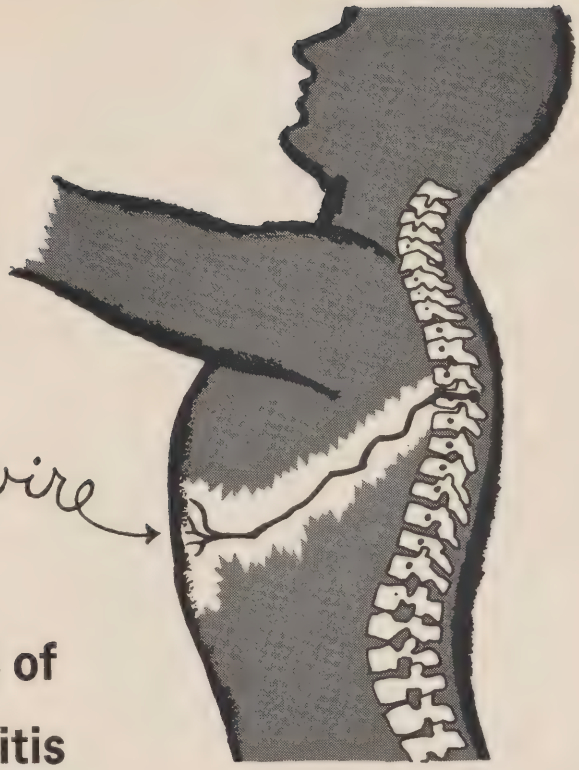
DR. OTTO N. GLESNE, of Fort Dodge, Iowa, has been appointed college physician and director of the health service at St. Olaf College, Northfield. Dr. Glesne graduated from St. Olaf in 1921, and took his medical degree at the University of Minnesota in 1926. He is a founding member of the American College of Obstetrics and Gynecology.

* * * *

DR. ROBERT L. HEGRENES joined the staff of the River's Edge Medical Clinic, Farmington, in July. Dr. Hegrenes

(Continued on page 24A)

Like a Red Hot wire



the Searing *Pain* of Inflammatory Neuritis

PROTAMIDE®

colloidal solution of denatured proteolytic enzyme

provides the *selective* fast-acting relief . . .

Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

- relief of inflammatory pain (non-traumatic) is prompt—particularly when administered early.[1-4]
- disability time is shortened from weeks to days.[7]
- so specifically effective is Protamide that a positive response is diagnostic of inflammatory neuritis.[3,4]
- prompt relief is observed even in ophthalmic herpes zoster.[5,6]
- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
- consistently described as the therapy of choice.[1,3-6]

Administration:

In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

—Boxes of 10 ampuls, 1.3 cc. each.—

References: (1) Baker, A. G.: Penn. Med. J. *63*:697-698 (May) 1960. (2) Smith, R. T.: New York Med. *8*:16-19 (Aug. 20) 1952. (3) Smith, R. T.: Med. Clin. N. America (March) 1957. (4) Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. *54*:1249-1252 (Nov.) 1955. (5) Sforzolini, G. S.: Arch Ophthal. *62*:381-385 (Sept.) 1959. (6) Shupala, E.: W. Virginia Med. J. *56*:191-193 (June) 1960. (7) Xander, G. W.: Western Med. *1*:14-17 (Sept.) 1960. (8) Combs, F. C., and Canizares, O.: New York J. Med. (Mar. 15) 1952, pp. 706-708. (9) Marsh, W. C.: U.S. Armed Forces Med. J. *1*:1045 (Sept.) 1950. (10) Love, T. R.: Rocky Mountain Med. J. *50*:873 (Nov.) 1953.

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FREE PARKING

NEWS BRIEFS

(Continued from page 22A)

graduated in 1962 from the University of Minnesota Medical School, Minneapolis.

* * * *

DR. FREDERICK L. SCHADE, obstetrician and gynecologist at the Worthington Clinic for the past twenty-nine years, retired during July and has moved to California. Dr. Schade graduated from the University of Minnesota School of Medicine in 1935. He is a member of the Central Association of Obstetricians and Gynecologists and of the American College of Obstetricians and Gynecologists.

* * * *

DR. WILLIAM N. SPELLACY, head of the department of obstetrics and gynecology at the University of Minnesota, reports his department has been awarded a public health service grant of $13,190 to study levels of plasma, insulin, and growth hormone in pregnancy.

* * * *

DRS. ROBERT W. MERRILL and JAMES R. SCHUFT have discontinued the practice of medicine in Morris. Dr. Merrill, general practitioner, has accepted a fellowship in physical medicine and recreation at the University of Minnesota Hospitals, Minneapolis. Dr. Schuft, general practitioner in the Watson and Schuft Clinic for the past five years, has undertaken training in radiology at the Charles T. Miller Hospital, St. Paul.

* * * *

DR. ERNEST A. OLSON of Pine Island, has received a plaque from the people of Pine Island in appreciation of his forty-one years of service to the community. A general practitioner, he obtained his medical degree in 1924 from the University of Minnesota.

* * * *

DR. HAROLD W. HENRY, formerly of Hinckley, has joined Dr. Martin S. Munson, of Moose Lake, in the general practice of medicine. Dr. Henry will work in the Lakeside Clinic, Moose Lake.

* * * *

DR. WARNER G. WORKMAN, 77, a native of Tracy and a practicing physician-surgeon in that community for the past fifty-two years, retired in July. He graduated in 1912 from the University of Minnesota Medical School. For more than fifty years he was district surgeon for the C & NW railroad.

* * * *

DRS. ROBERT H. CONLEY, BENJAMIN R. GEURS, and ALOIS M. SCHEIDEL, all internists, have opened a new medical clinic in Mankato. Dr. Conley and Dr. Geurs have been practicing together for fifteen years; Dr. Scheidel joined them ten years ago.

* * * *

DRS. ROBERT C. PFEILER and HENRY HUTCHINSON, psychiatrists, recently resigned from the state's mental health program. Dr. Pfeiler, former director of Minnesota Community mental health services, is currently exploring a number of assignment possibilities in social psychiatry in the Federal service. Dr. Hutchinson, superintendent of Moose Lake State Hospital for the mentally ill since 1947, has accepted an appointment as staff psychiatrist at the Veterans Administration Hospital, St. Cloud.

* * * *

DR. HERBERT VON ROHR HEISE, general practitioner, has been reelected for another one-year term as president of

the medical staff of Community Memorial Hospital, Winona. Others reelected are Dr. F. J. Vollmer, vice-president, and Dr. Louis J. Wilson, secretary.

* * * *

DR. EVERETT J. SCHMITZ, general surgeon, has been elected chief of the St. Cloud Hospital medical staff. Dr. Edward M. LaFond, orthopedic surgeon, has been elected vice-chief of staff.

* * * *

DR. ARNOLD M. BERG, former Roseau physician, has begun practice with the Falls-Starekow Clinic in Thief River Falls.

* * * *

DR. ROBERT I. GRUYS, general surgeon from Wells, has received the degree of fellow in the International College of Surgeons. Dr. Gruys graduated in 1947 from the University of Minnesota Medical School.

* * * *

DR. PAUL W. GERSTER, 1958 graduate of the University of Minnesota Medical School, has been assigned chief of obstetrics and gynecology at the U.S. Army Hospital at Fort Hood, Texas. Major Gerster is formerly of Farmington.

* * * *

DR. RICHARD T. HENRY has discontinued practice in Crosby in order to accept a position in Merritt Island, Fla., as medical officer with Trans World Airlines at the John F. Kennedy Space Center.

* * * *

DR. JAMES KVALE is the first physician in the new clinic at Atwater, financed by the village and surrounding area. The clinic will eventually house two doctors. Dr. Kvale, 29, is a native of Duluth and a graduate of George Washington University and the University of Pennsylvania.

* * * *

DR. HAROLD M. GRANING, formerly of Minneapolis and now assistant surgeon general of the United States, is heading a five-man delegation of American physicians on a three-week tour of Soviet hospitals. Dr. Graning received his medical degree from the University of Minnesota in 1938.

* * * *

DRS. LA RUE VERLOY DAHLQUIST and DARREL W. SIEBERT have opened practice in Pipestone. Dr. Dahlquist is associated with Dr. Frank E. Boyd in the Boyd Clinic, and Dr. Siebert is in private practice.

* * * *

DR. JAMES B. NIXON of Deerwood, associated with the Cuyuna Range Clinic in Crosby, has been appointed Crow Wing county coroner. He replaces Dr. Maurice Meller of Brainerd, who resigned in January.

* * * *

DR. WARREN M. DODGE, JR., 64, a native of Farmington and for thirty-two years an ophthalmologist in Battle Creek, Mich., has retired. Dr. Dodge graduated in 1927 from the University of Minnesota Medical School. He is a member of the American Academy of Ophthalmology and Otolaryngology and the American College of Surgeons.

* * * *

DR. ARTHUR H. BULBULIAN, director of the Mayo Medical Museum, and member of the Mayo Clinic staff, presented 5 scientific exhibits at the recent annual convention of the American Medical Association.

(Continued on page 26A)



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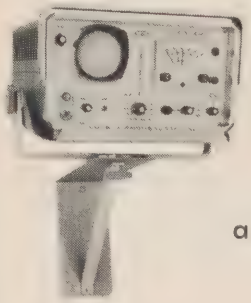
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NEWS BRIEFS

(Continued from page 25A)

DR. LAURENTIUS O. UNDERDAHL, associate professor of clinical medicine of the Mayo Graduate School of Medicine, University of Minnesota, has been named president-elect of the American Diabetes Association.

* * * *

DR. HADDON M. CARRYER, head of a section of medicine at the Mayo Clinic, discussed the use of corticosteroid drugs in the treatment of asthma at a meeting of allergy specialists at the American Medical Association annual convention.

* * * *

TEN NEW MEMBERS have been added to the staff of the Mayo Clinic. Seven are presently residents of the Mayo Graduate School of Medicine, University of Minnesota: Drs. James B. Bassingthwaighte, consultant in the section of physiology; M. Robert Wilson, consultant in the section of psychiatry; Carlo M. Veneziale, consultant in internal medicine; Richard O. Lundborg, consultant in the section of anesthesiology; J. Paul Marcoux, consultant in internal medicine; Jean Reiher, consultant in the section of physiology; and Sait Tarhan, consultant in the section of anesthesiology.

Other new appointees include Dr. Lillian R. Elveback, former Mayo Graduate School resident, consultant in the section of biometry and medical statistics; Dr. Donald R. Krabill, also a former resident, consultant in the section of anesthesiology; and Dr. Gerald J. Gleich, graduate of the University of Michigan Medical School, consultant and clinical investigator in the section of microbiology.

* * * *

DR. RUSSELL G. SPRAGUE, of the Mayo Clinic, has received the Banting Memorial Award from the American Diabetes Association for his research in metabolic diseases. In 1954 Dr. Sprague received the Banting award for studies of diabetes.

* * * *

DR. HOWARD F. POLLEY, Mayo Clinic specialist in rheumatic diseases, has been awarded an honorary doctor of science degree from Ohio Wesleyan University, Delaware, his undergraduate alma mater.

* * * *

FIVE CONSULTANTS in the Mayo Clinic and faculty members of the Mayo Graduate School of Medicine, University of Minnesota, have been promoted from associate professor to professor: Dr. Donald R. Nichols and Dr. L. Emmerson Ward, professors of clinical medicine; Dr. Oliver H. Beahrs, professor of surgery; Dr. Eugene Ackerman, professor of biophysics; and Dr. Richard K. Winklemann, professor of dermatology. Dr. Leonard T. Kurland, head of the section of biometry and medical statistics in the Mayo Clinic, has been appointed professor of biostatistics.

* * * *

THE AMERICAN ASSOCIATION OF AUTOMOTIVE MEDICINE, in cooperation with the Mayo Clinic and Mayo Foundation, will sponsor a program on automotive safety and accident prevention Oct. 22-23 at the clinic. Registration fee is $20. Details can be secured by writing Postgraduate Courses, Mayo Clinic, Rochester, Minn.

* * * *

DR. NORMAN A. CHRISTENSEN, internist at the Mayo Clinic, and designer of the medical identification cards now used by Mayo patients, recently taped a discussion of the cards for Monitor, NBC's nationwide radio network program.

NEWS BRIEFS

DR. HERMAN J. MOERSCH, emeritus member of the Mayo Clinic staff and director of education and research for the American College of Chest Physicians, has received the college's annual medal for meritorious service in diseases of the chest.

* * * *

DR. JAMES C. CAIN, consultant in medicine in the Mayo Clinic, and professor of clinical medicine in the Mayo Graduate School of Medicine, University of Minnesota, has been named chairman of the National Advisory Committee on Selective Service by President Lyndon B. Johnson. Dr. Cain, a colonel in the reserve corps, Army Medical Corps, received his M.D. from the University of Texas in 1937, and was a fellow in medicine in the Mayo Graduate School of Medicine in 1940 and 1941 and from 1946 to 1948. He has been a member of the staff of the Mayo Clinic since 1948.

* * * *

DR. JOHN J. GALLIGAN, chief of staff of Children's Hospital, St. Paul, and Dr. Martha J. Burke-Strickland, director of medical education, have received word that the hospital's two-year residency program in pediatrics has been provisionally approved by the American Academy of Pediatrics, the American Board of Pediatrics, and the Council on Medical Education. The program is affiliated with the University of Minnesota.

* * * *

FIVE MEMBERS OF THE STAFF of the Mayo Clinic have been elected officers of sections of the American Medical Association. Dr. Lowell L. Henderson was elected secretary of the section on allergy; Dr. Lloyd G. Bartholomew, secretary of the section on gastroenterology; and Dr. Gordon M. Martin, secretary of the section on physical medicine and rehabilitation. Dr. Archie H. Baggenstoss, secretary of the section on pathology and physiology for the past three years, was elected vice-chairman. Dr. David C. Utz was elected assistant secretary of the section on urology.

* * * *

DR. GEORGE M. JOHNSON, formerly a resident in pediatrics at the Mayo Foundation, is now located in Bismarck, N.D.

* * * *

DR. WILLIAM R. REMINE, head of a section of surgery at the Mayo Clinic, and associate professor of surgery in the Mayo Graduate School of Medicine, University of Minnesota, has been elected president of the Minnesota Surgical Society.

South Dakota

DR. C. ROGER HERBRANDSON, Sioux Falls, has been named to the staff of the Homestake Hospital in Lead, S.D. Dr. Herbrandson is a 1964 graduate of the University of Minnesota Medical School, and recently completed his internship at the Sioux Valley Hospital in Sioux Falls.

* * * *

DR. ALBERT C. MARTIN, a general practitioner, has joined the Donahoe Clinic of Sioux Falls and is in charge of the Luverne, Minn., offices. Dr. Martin has practiced in Luverne for fifteen years and will occupy his same offices. He said he joined the Donahoe Clinic in order to be able to offer his patients the services of the clinic's specialists.

* * * *

DR. LOUIS W. KARLEN has begun practice in Madison in association with Dr. George E. Whitson and Dr. Howard

(Continued on page 28A)



MAIN BUILDING — One of 8 Units in "Cottage Plan"

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WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

INTERNIST—Board Certified or qualified for Multispecialty 6-Man Group in midwestern community with 250-bed hospital. Salary or percentage first year, then progressively leading to full partnership. Reply Box 32 c/o Journal Lancet.

PEDIATRICIAN—Board Certified or qualified for Multispecialty 6-Man Group in midwestern community with 250-bed hospital. Salary or percentage first year, then progressively leading to full partnership. Reply Box 33 c/o Journal Lancet.

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SACRED HEART, MINNESOTA has been without a doctor since 1961. General practitioner will find suitable building in 700 pop. village, modern hospital 10 miles away; progressive, stable community in west central part of state. Good school, churches. Good family environment. Call or write Rev. Robert Bardy, Telephone 765-2547, Sacred Heart, Minn.

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NEWS BRIEFS

(Continued from page 27A)

R. Wold. Dr. Karlen graduated from the University of Kansas School of Medicine, Kansas City, Kan., and served his internship at Kansas City General Hospital, Kansas City, Mo.

* * * *

DR. BRUCE H. ALLEN, an ear, nose, and throat specialist, has joined the staff of the Rapid City Medical Center. Dr. Allen graduated from the Temple University School of Medicine, Philadelphia, in 1955, and served nearly three years as a flight surgeon in the U.S. Air Force. From 1961 to the present, he took postgraduate training in otorhinolaryngology at Henry Ford Hospital, Detroit, Mich.

Deaths . . .

DR. MARTIN A. NORDLAND, JR., 45, general surgeon, died May 30. Dr. Nordland graduated from the University of Minnesota Medical School in 1945 and served a medical fellowship at the Mayo Clinic, Rochester. He was a member of the American College of Surgeons.

* * * *

DR. ARTHUR F. BRATRUD, 78, died May 31 in Minneapolis where he had practiced surgery from 1920 to his retirement in 1963. Dr. Bratrud was an assistant professor of surgery at the University of Minnesota Medical School, from which he graduated in 1912. He was a staff member at Asbury Methodist and Mt. Sinai hospitals in Minneapolis.

* * * *

DR. THOMAS W. MURPHY, 87, long-time Bristol physician, died during May. Dr. Murphy received his medical degree from the State University of Iowa, Iowa City, in 1903. He was a member of the American Medical Association and of the South Dakota Medical Association.

* * * *

DR. DANIEL C. DARROW, 70, a native of Fargo and a resident of Wilmington, N.C., died July 2 in North Carolina. Dr. Darrow, a pediatrician, was a graduate of Cornell University and Johns Hopkins School of Medicine, and a member of the American Academy of Pediatrics, the American Pediatric Society, and the American Society for Clinical Investigation.

* * * *

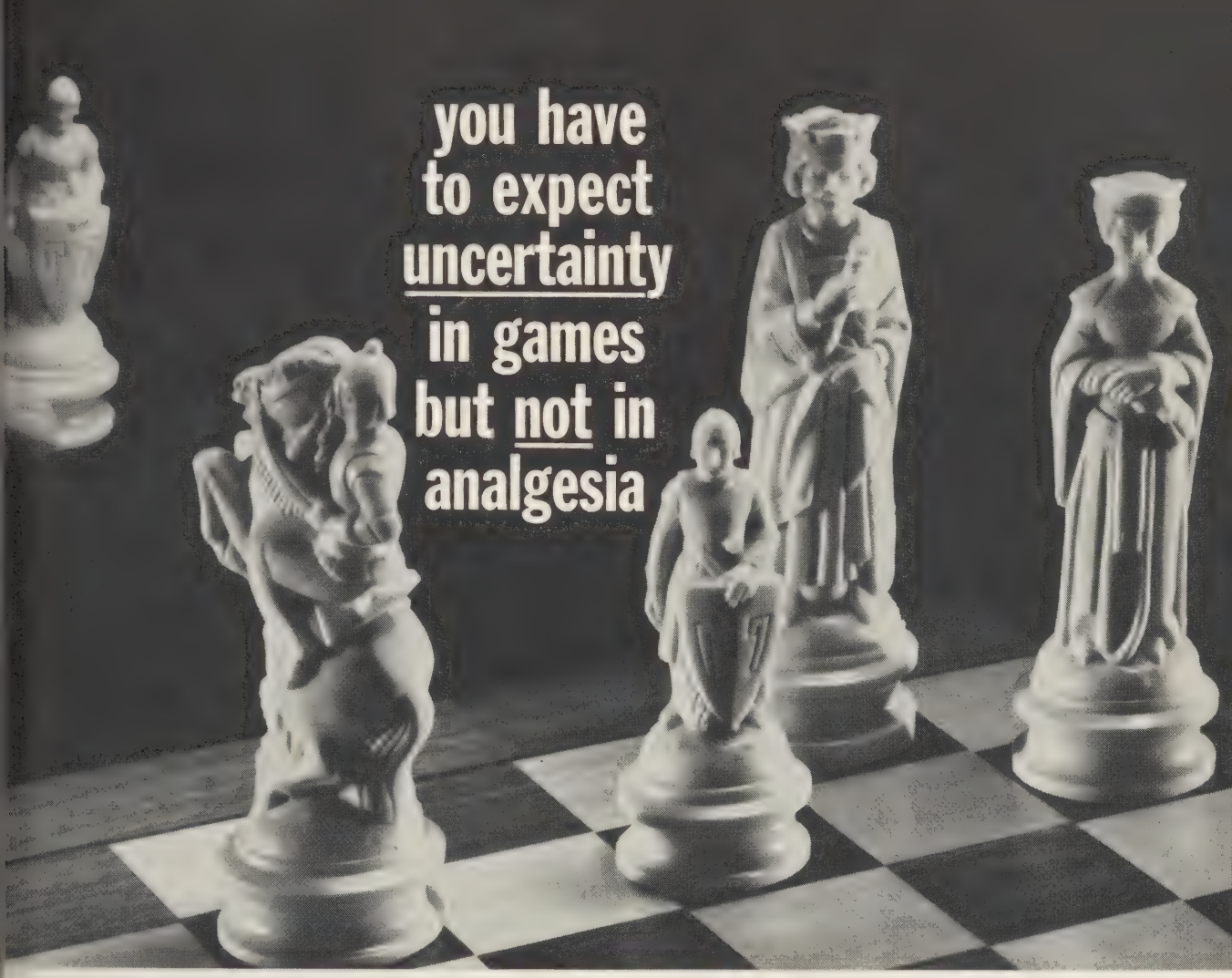
DR. JOSEPH A. HILTS, 56, of Mandan, N.D., died June 28 in his home at New Salem after a long illness. Dr. Hilts, a general practitioner, received his medical degree in 1938 from the University of Manitoba, Winnipeg, Canada.

* * * *

DR. NORVIN R. SMITH, 52, physician and surgeon at Hastings State Hospital, Minn., died in his office at the hospital July 14. Dr. Smith, a 1935 graduate of the University of Nebraska College of Medicine, was a member of state and national medical associations and the American Legion.

* * * *

DR. LEWIS S. JORDAN, 69, of Granite Falls, Minn., died July 17. Dr. Jordan, a specialist in pulmonary diseases, graduated in 1926 from Eclectic Medical College, Cincinnati, Ohio. He was a member of the American College of Chest Physicians and the American Thoracic Society.



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soothing decongestant and expectorant



relieves cough
nasal drip
congestion
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bright red, pleasant-tasting, raspberry-flavored syrup

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Exempt Narcotic.

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Phenylephrine hydrochloride	5 mg.
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Vitamin C	100 mg.

Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

Indications: Cough, congestion, headache, discomfort and muscular aches and pains in coryza, rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, bronchitis, grippe, influenza and pneumonia.

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with the option of b.i.d. dosage



The Journal-Lancet Volume 85, No. 10, OCTOBER 1965

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Lehmann, H. E., Canad. Psychiat. Assn. J. *4(S)*: 1-12, 1959



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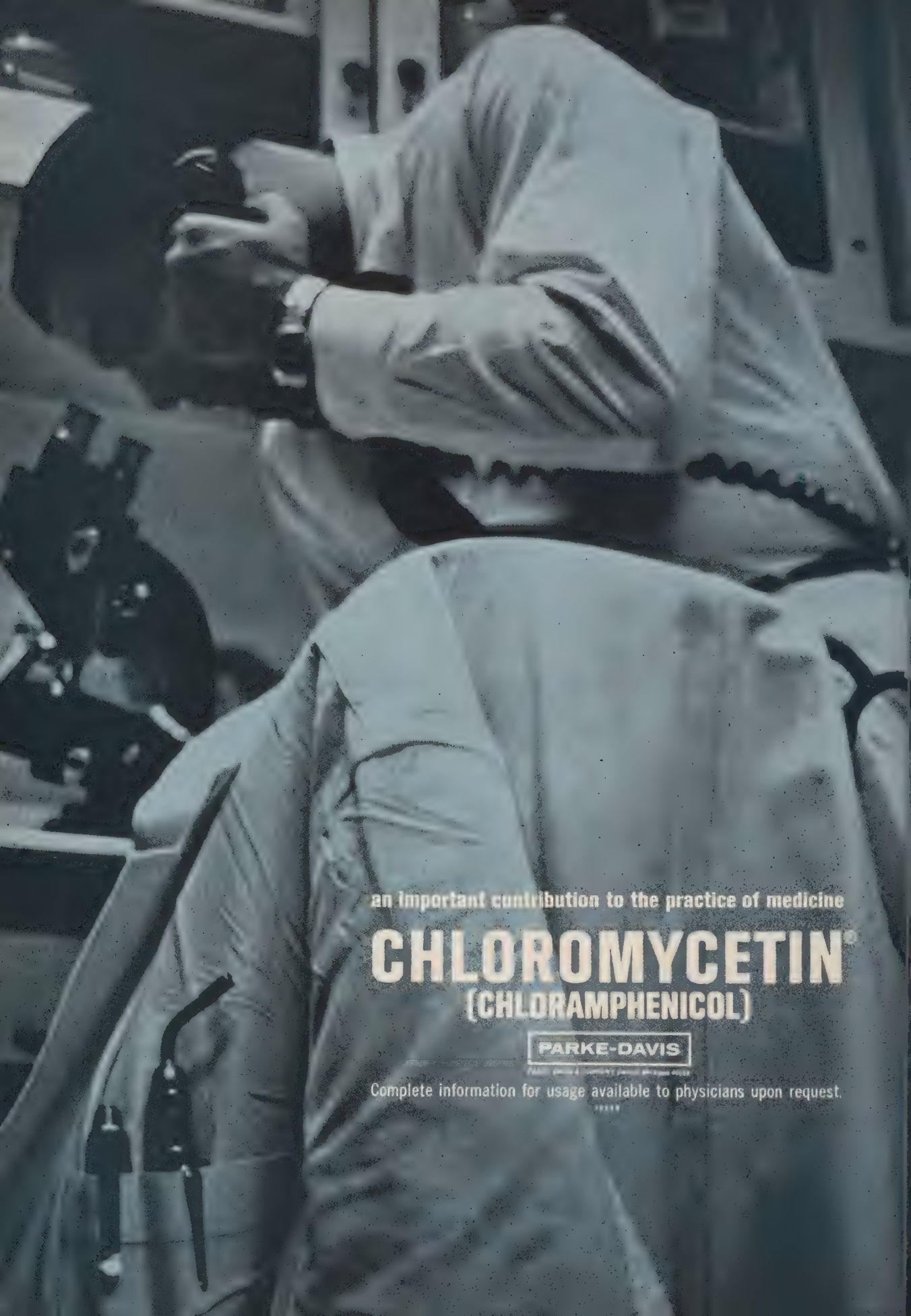
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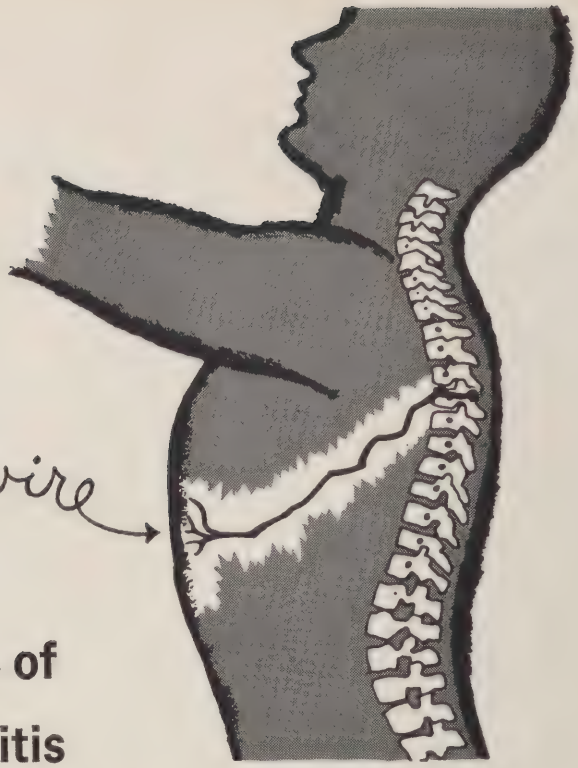
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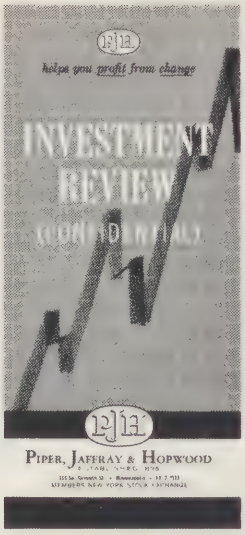
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In November, THE JOURNAL-LANCET will present the third in a series of special issues devoted to pediatrics. The papers from the Children's Memorial Hospital, University of Oklahoma Medical Center, are a sample of the diverse and wide-ranging clinical and research activities which typify a children's hospital of today and its activities in child health. Guest editor is Dr. Harris D. Riley, Jr., head of the department of pediatrics, University of Oklahoma. Contributions include:

- **Idiopathic Thrombocytopenic Pupura in Children: An Analysis of 25 Cases,** by Theresa B. Haddy, M.D.
- **Tetanus: Epidemiologic and Clinical Aspects of 72 Cases,** by Howard Paxton, Jr., M.D., and Harris D. Riley, Jr., M.D.
- **Coexistent Cranial and Spinal Defects with Hydrocephalus in Five Infants: The Etiology and Significance of Craniolacunia in these Defects,** by J. T. Jabbour, M.D., and R. D. Vallion, M.D.
- **Interrelationships between Pathogenic Bacteria and the Pulmonary Mucus in Cystic Fibrosis,** by K. H. Nida, M.S., and E. C. Bracken, Ph.D.
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- **Cardiovascular Aspects of the Collagen Diseases,** by W. M. Thompson, Jr., M.D.
- **Clinical Evaluation of Noisy Respiration in Infancy,** by James B. Snow, Jr., M.D.
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- **Language Disorders in Children,** by Sylvia O. Richardson, M.D.
- **The Relative Role of Heredity and Environment in Congenital Heart Disease: A Review,** by Russell F. Shaw, M.D.
- **Changing Concepts of Pediatric Uroradiology,** by Charles E. Shopfner, M.D.
- **Pediattric Grand Rounds: Hyperthyrodism, Diabetes Mellitus, and a Myasthenia Gravis-Like Syndrome in a Seven-Year-Old Girl**

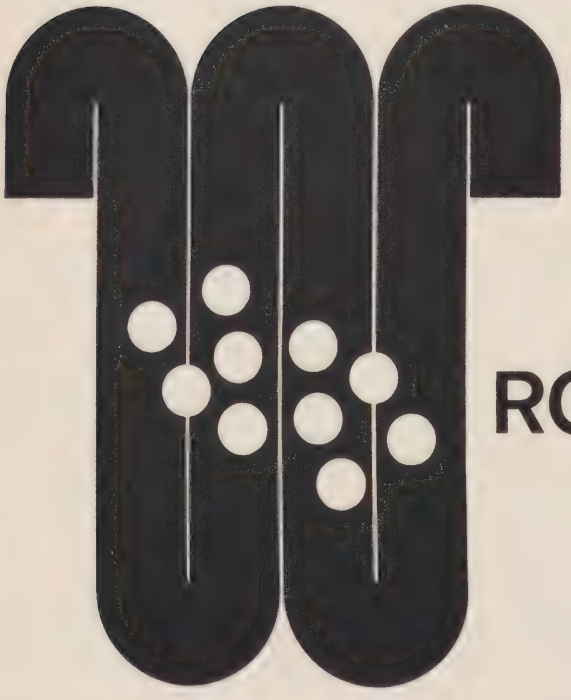
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Carcinoma of the Esophagus

A Twelve Year Study

MARTIN J. LOEB, M.D.

Minneapolis

THE BASIS for this report is a review of 111 cases of histologically proven cancer of the esophagus during a twelve year period from 1952 to 1963. Trends in therapy have changed over these years and have contributed to a somewhat improved outlook.

MATERIALS AND METHODS

All patients discharged from the Minneapolis Veterans Hospital from January 1952 to December 1963 with a diagnosis of cancer of the esophagus were included in this study. Some had initial evaluation at other hospitals and were then referred for definitive therapy. After diagnosis by esophagogram and esophagoscopy, a decision was made as to the preferred mode of therapy. Before 1959 this consisted of partial esophagectomy and esophagogastrostomy; however, since that date total esophagectomy with colon interposition in 2 stages has been practiced.

RESULTS

The youngest patient in the series was 40 years old and the oldest 85. As indicated in figure 1, most were in the age range of 50 to 69 years old. Although the male-female ratio usually reported is 4 to 1,[1] as would be expected in a veterans hospital, all patients in this series were male. Nineteen malignancies were in the upper esophagus, 52 were in the midesophagus, 34 were in the lower esophagus, and 6 originated in the mid-lower or mid-upper area (Table 1). This is consistent with other reports in which the mid-esophagus predominates slightly as the site of carcinoma.[2]

There were 107 cases of squamous-cell carcinoma, 2 leiomyosarcoma, 1 undifferentiated carcinoma, and 1 adenocarcinoma from the mid-esophagus. Other adenocarcinomas from the cardio-esophageal junction were omitted since their esophageal origin was dubious.

Unless there were contraindications, surgery was the recommended treatment in lesions of the lower two-thirds of the esophagus. Lesions in the upper third of the gullet were generally treated by radiation with the exception of 2 cases performed in the early years of this study. The causes for inoperability were, in most instances, absolute and are listed in table 4. A total of 62 (55%) were therefore explored and 40 (36%) found to be resectable. With a few exceptions, the remainder had palliative radiation. The average survival for those patients having no treatment was 3.2 months, while those receiving radiation lived 6.4 months. This is depicted graphically in figure 2.

An attempt was made to analyze pathological reports regarding extent of tumor and positive nodes. Two-thirds of the resected cases showed positive nodes, but no distinct correlation between survival and positive nodes could be

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TABLE 1

LOCATION OF ESOPHAGEAL CANCER

Upper	19
Mid	52
Low	34
Mid and low	4
Mid and upper	2
Total cases	111

TABLE 2

HISTOLOGY OF ESOPHAGEAL CANCER

Squamous cell	107
Leiomyosarcoma	2
Undifferentiated	1
Adenocarcinoma	1
Total cases	111

TABLE 3

MODE OF THERAPY

Surgery	33
Surgery and radiation	7
Exploration and radiation	14
Exploration	8
Radiation	33
Support	15
Chemotherapy	1
Total cases	111

TABLE 4

REASON FOR INOPERABILITY

Location and extent	12
Positive nodes	11
Cachexia	10
Paresis of vocal cord	5
Metastases	5

TABLE 5

SURGICAL RESULTS OF RESECTED CASES, 1952 to 1963

Year	*No. cases*	*Surgical mortality*	*Percent*
1952 to 1957	18	8	44.4
1958 to 1963	22	4	18.2
Total	40	12	30.0

made. In only 8 of the 40 resected cases was tumor confined to the esophageal musculature. The remainder showed penetration through the entire wall. As might be expected, survival of the 8 patients was well above average.

There are 3 patients now free of disease at 22, 39, and 96 months, respectively. Two men had total esophagectomies and the third had a partial esophagectomy and esophagogastrostomy.

CASE HISTORIES

1. This 52-year-old patient entered the hospital with complaints of substernal chest pain of six months' duration, dysphagia of six weeks' duration, and a 20 lb. weight loss. A midesophageal lesion was discovered. Biopsy showed squamous-cell carcinoma. Total esophagectomy was performed and the tumor appeared to be localized. Out of 14 nodes recovered, none were positive. Right colon transplant was performed six weeks later. Necrosis of the distal colon necessitated construction of a short skin tube. He is twenty-two months past operation and free of disease.

2. This 57-year-old patient entered the hospital with difficulty in swallowing and substernal soreness of two months' duration. There was a concomitant 30 lb. weight loss. A midesophageal carcinoma was resected by total esophagectomy. The lesion was through the thickness of the esophageal wall, but there was no further spread. One of the 2 nodes was positive for cancer. Postoperatively, he developed a small wound infection which delayed colon transplant. This was finally performed. The patient is now doing well thirty-nine months after primary resection. He has had no difficulty swallowing.

3. This 59-year-old patient was seen because of an episode of nausea and vomiting. Upper gastrointestinal series revealed a low esophageal lesion which proved to be squamous-cell carcinoma. A partial esophagectomy and esophagogastric anastomosis was performed. The tumor was localized and superficial and did not invade muscle in any section. There were no positive nodes. The patient is well eight years after surgery.

Two other patients lived twenty-four and thirty-eight months, respectively, and died free of their disease. They, too, had total esophagectomies with colon replacement.

The surgical results have shown improvement over the years as indicated in table 5. There has been a decrease in the operative mortality from 44% in the first six year period 1952 to 1957, to 18.2% in the second six year period (Table 5). There have been no attempts at surgery of the upper esophagus in the last six years.

From 1959 total esophagectomy has been recommended in resectable cases and since then 17 such resections have been done. There have been 3 deaths (17.6%). After recovering from the first stage procedure, colon interposition is attempted. Unless there are complications, the interval between stages is four to six weeks. Three patients were not suitable for the second stage because of evidence of metastases.

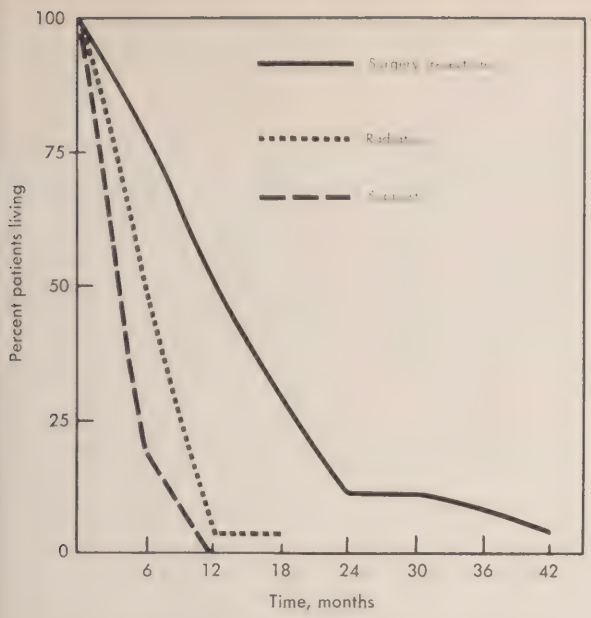


Fig. 1. Age distribution of patients with esophageal cancer

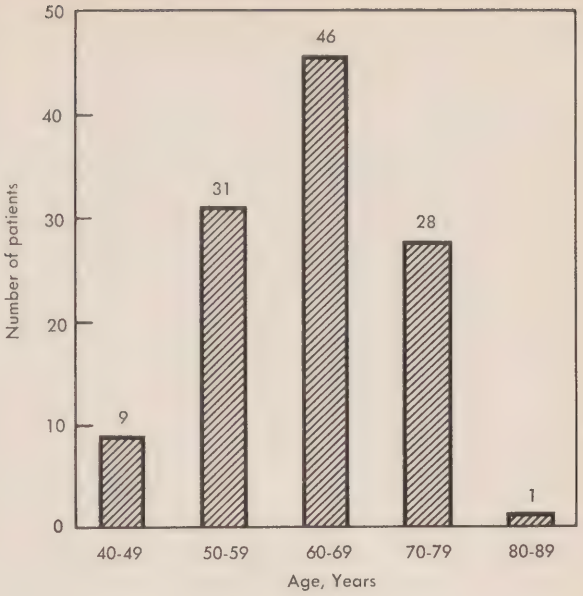


Fig. 2. Survival time, all types of treatment.

In 11 patients retrosternal colon interposition was carried out. Whenever possible the left colon has been used and is considered preferable simply because length is more readily obtainable. However, the right colon has been used with success. There was 1 death due to necrotic colon and secondary septicemia. In 3 patients the procedure was carried out without difficulty. Four had stenosis of the proximal esophagocolon anastomosis. In 3 patients in whom the right colon was used, difficulty was encountered in length. Two of these patients had subsequent skin tubes to bridge the gap. The last died of recurrent disease before further repair could be done.

DISCUSSION

Since Torek first reported a successful resection of carcinoma of the esophagus in 1913, surgery has generally been considered the best hope for this disease. We approached this initially by a partial resection and esophago-gastric anastomosis. However, it has been noted that longitudinal spread along the esophagus is commonly missed in such limited resections.[3] Because of this and the potential multicentricity of the disease, total esophagectomy is recommended.

Recently, the place of X-ray as an adjunct to surgery has been investigated,[4] and in this area may lie the hope for better survival.[5,6] In this study 6 out of the 40 patients resected underwent postoperative irradiation because it was felt at the time of surgery that tumor was left behind. This did not seem to affect survival rates.

Although this report shows a low five-year survival, there is room for some optimism. First, the mortality for esophagectomy has diminished markedly. Second, since total esophagectomy was instituted, long-term survivors and those dying free of this disease have been more frequent. Third, there is evidence that preoperative irradiation may increase resectability. However, further study must be given to this aspect of treatment.

SUMMARY

1. A series of 111 cases of carcinoma of the esophagus is presented.

2. Resection was carried out in 40 patients with a mortality of 44.4% for the period 1952 to 1957 and 18.2% for the period 1958 to 1963.

3. Total esophagectomy with second stage retrosternal colon interposition is recommended.

4. The place of adjunctive preoperative X-ray should be evaluated.

I wish to thank Dr. Edward W. Humphrey for his many helpful comments and suggestions.

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Influence of Diet upon Nonfasting Blood Sugar and Glucose

Reexamination of the Effects of a Relatively Low-Refined Carbohydrate, High-Protein Diet

E. CHERASKIN, M.D., and W. M. RINGSDORF, JR., D.M.D.
Birmingham, Alabama

A RECENT REPORT[1] indicated 3 interesting results following the institution of a three-day relatively low-refined carbohydrate, high-protein diet in the human being. First, relatively high nonfasting blood sugar and blood glucose levels declined. Second, relatively low blood sugar and blood glucose scores rose. Last, the final blood sugar and blood glucose values settled within a narrow range more restricted than the conventional physiological parameters. Because of the importance of diet to diabetes mellitus and the even greater significance of carbohydrate metabolism to host resistance and susceptibility in many other presumably nondiabetic disease states,[2–17] this report is a confirmatory check on the previously described findings.

METHODS

Forty presumably healthy dental students participated in this study. On Monday of the week, the nonfasting, two-hour postprandial blood sugar[18] and blood glucose[19–21] were determined. The subjects were then instructed to eliminate, as far as possible, refined carbohydrates from the diet. The recommendation was also made that protein intake be increased. Nonfasting, two-hour postprandial blood sugar and blood glucose were remeasured Friday of the same week by the same technician with no knowledge of the earlier findings. The mean laboratory (technical) error in determining blood sugar and glucose was found to be approximately 3 mg. percent.

RESULTS

The table presents the means and standard deviations for both the pre- (initial) and postdietary (final) blood sugar and blood glucose analyses. Although the mean values did not change significantly during the experimental period, uniform differences did occur in the individual blood sugar and blood glucose levels.

When plotted graphically (Fig. 1) the evidence suggests that blood sugar levels above 100 mg. percent decreased while those below 100 mg. percent increased. This trend toward homeostasis is underscored by a significant ($P < 0.001$) coefficient of correlation ($r = -0.642$).

The elevations of low and reduction in high blood glucose levels during the three-day dietary interval were even more orderly. The line of regression in figure 2 indicates that blood glucose levels tended to migrate toward 80 mg. percent. The validity of this observation is emphasized by a very significant ($P < 0.001$) correlation coefficient ($r = -0.721$).

DISCUSSION

The evidence from these 40 subjects indicates that, under the influence of a relatively low-refined-carbohydrate, high-protein dietary, there is a tendency for the two-hour postprandial blood sugar and glucose levels to approach 100 and 80 mg., respectively. These conclusions are even more interesting in view of the fact that, according to present physiological standards[22,23] for blood sugar and glucose, all 40 students were within so-called "normal limits."

These findings in healthy young men confirm the earlier observations in 683 patients[1] that nonfasting blood sugar by the Folin method[24] tends to seek a level near 100 mg. percent following a three-day low-refined carbohydrate, high-protein

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EFFECT OF A THREE-DAY RELATIVELY LOW-REFINED CARBOHYDRATE, HIGH-PROTEIN DIET UPON NONFASTING BLOOD SUGAR AND GLUCOSE

	Blood sugar (Folin-Wu method)	*Blood glucose (Somogyi-Nelson method)*
Sample size	40	40
Initial mean scores	96.6	78.6
Initial standard deviations	13.4	13.5
Final mean scores	96.4	78.2
Final standard deviations	12.0	11.0
Significance of difference of means	=0.500	=0.500
Significance of difference of variances	=0.250	=0.100
Correlation of initial scores with differences from initial scores at second visit	—0.642	—0.721
Significance of correlation coefficient	<0.001	<0.001

diet regimen. This is borne out in the earlier report by a significant ($P < 0.001$) correlation coefficient of —0.840 between the initial blood sugar and the amount of blood sugar change after three days.

Thus, the factors controlling carbohydrate metabolism seem to be more precise when gluconeogenesis from protein sources is encouraged. This statement is further corroborated by an analysis of blood sugar levels following isoglucogenic quantities of protein and carbohydrates in healthy and diabetic individuals.[25]

The significance of these small but orderly changes in carbohydrate metabolism to host resistance and susceptibility is gaining importance as evidenced by the published literature.

The possibility that multiple sclerosis may be a disorder of carbohydrate metabolism has been proposed.[8,9,26] Sawyer[7] treated 7 multiple sclerosis patients with tolbutamide. In 6 of the participants a placebo was alternated with the tolbutamide. The patients were also alternated between regular, high carbohydrate, and diabetic diets while on tolbutamide or placebo medication. Sharp clinical improvement followed tolbutamide treatment except when a high-carbohydrate diet was instituted. Clinical exacerbation also followed placebo supplementation. A point clearly made by the author[7] is that a low-carbohydrate diet yielded favorable clinical results.

A number of investigators have concluded that a significant correlation prevails between atherosclerosis and carbohydrate metabolism. Waddell and Field[12] report that 95% of a series of atherosclerotic patients showed an abnormal, if not classically diabetic, carbohydrate metabolism picture.

There are now some reports suggesting a relationship of gout to carbohydrate metabolism. McKechnie[27] found an incidence of abnormal glucose tolerance in 59.6% of 47 Natal Indians with gout and hyperuricemia.

These illustrations of presumably nondiabetic disease states all have in common a disturbance, generally mild, in carbohydrate metabolism. Our findings suggest that significant changes follow dietary correction. It would, therefore, be appropriate to treat some of these disease states with the diet reported here. If the hypothesis set

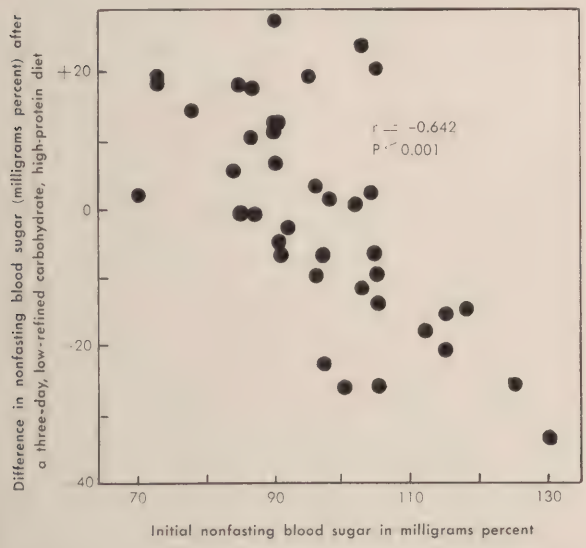


Fig. 1. Comparison of initial nonfasting blood sugar (abscissa) and difference from initial (ordinate) after a three-day low-refined carbohydrate, high-protein diet

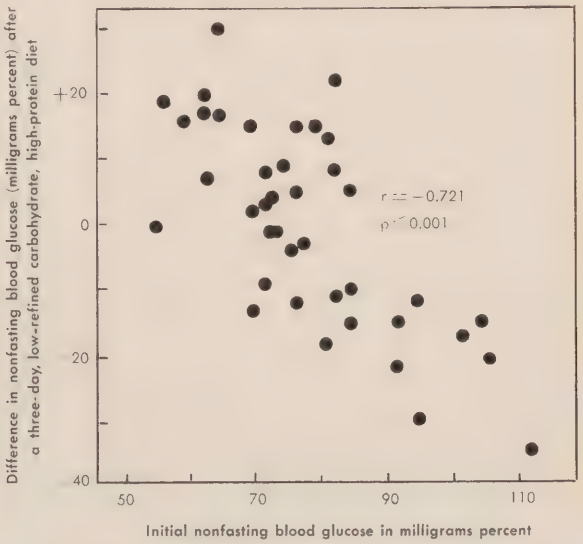


Fig. 2. Comparison of initial nonfasting blood glucose (abscissa) and difference from initial (ordinate) after a three-day low-refined carbohydrate, high-protein diet

forth here is valid, initial borderline blood glucose values should fall within a more narrow range with dietary change. More important, the reversible segment of the clinical picture should improve.

SUMMARY

A study of 40 healthy dental students subjected to a relatively low-refined carbohydrate, high-protein diet for three days revealed significant changes in nonfasting, two-hour postprandial blood sugar and glucose.

It would appear from these data that the physiological nonfasting blood sugar and glucose approximate 100 and 80 mg. percent, respectively.

The possible clinical applications of a low-refined carbohydrate, high-protein diet to so-called nondiabetic disease states, for example, gout, multiple sclerosis, and atherosclerosis, are discussed.

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Nuclear Medicine: Past and Present

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THE AVAILABILITY OF radioactive materials for use in medicine dates almost to the discovery of radioactivity by Bacquerel in 1896. In the fifty years that followed, very few radioactive materials other than radium and its related products were available to the practicing physician. Following World War II, there has been a steady increase in the availability of reactor-produced radioactive materials. This has been particularly true during the past decade during which rapid advances have been made in nuclear medicine.

The objective of nuclear medicine is to develop, evaluate, and propogate the use of radioactive materials in the diagnosis and treatment of disease. To this end, consideration must be given to the availability of radioactive materials, to the availability and performances of devices for measurement of radioactivity, and to the radiation hazard to patients and clinic personnel. Initially, practically all radioactive materials were available only from Oak Ridge National Laboratories. Gradually, commercial firms have taken over the preparation and distribution of radiopharmaceuticals so that today there are several hundred especially prepared radioactive materials available for use in medicine and medical research. There is no doubt that the number of radioisotopic preparations will be increased substantially in the future.

The rapid growth in availability of radioisotopes has been paralleled by rapid advances in nuclear instrumentation. Much attention has been given to instruments for study of the dynamic function of organs and for their visualization. Such things as cost, speed and reliability of obtaining data, versatility, and sensitivity have been major considerations in this development. Unfortunately, cost of certain of these devices is such that their use will likely be limited to clinics with a large patient volume. Nonetheless, there are instruments available, at costs which are within the budgets of most private hospitals and clinics, which will permit the performance of the majority of techniques of nuclear medicine.

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The sensitivity of nuclear instruments will determine in part the amount of radioactivity which must be administered to a patient in order to perform a particular study. This is, then, an important consideration because of our concern about radiation exposure of patients and personnel. In practically all tests currently being performed in our clinic, radiation exposure to the patient is significantly less than that associated with most X-ray procedures, particularly those which include fluoroscopy.

It is now well established that radioisotopes afford a convenient and reliable tool for the visualization and evaluation of the function of various body organs. Evaluation of thyroid, liver, and kidney function using radioisotopic tracers is well known. Likewise, the visualization of these organs as well as other body structures such as brain, bone, lung, heart, and pancreas is well established. In recent studies, we have also demonstrated parathyroid adenomas, salivary glands, orbital tumors, and the various compartments of the gastrointestional tract. The majority of this effort is directed toward demonstration of cancer or other disease at various body sites.

Some form of a crystal scintillation detector is used for all of these studies. For dynamic function tests, the rate at which radioactivity is received by the detector is of prime importance. This information is usually transmitted from the detector through a rate metering system and displayed on a strip chart recorder. Thus, the radioactivity as seen by the detector is plotted as a function of time. Extensive use of this technique is being made in the evaluation of kidney function in patients with hypertension, with some form of renal disease, or with renal transplants. Consideration is also being given to the evaluation of cardiac, hepatic, and splenic function.

Iodohippurate sodium (Hippuran®) labeled with I^{131} is conventionally used for renography. This material is cleared from the blood stream exclusively by rapid glomerular filtration (20%) and tubular secretion (80%). A normal renogram pattern is shown in figure 1. There are considered to be 3 characteristic segments to the renogram pattern. An initial spike usually lasting less

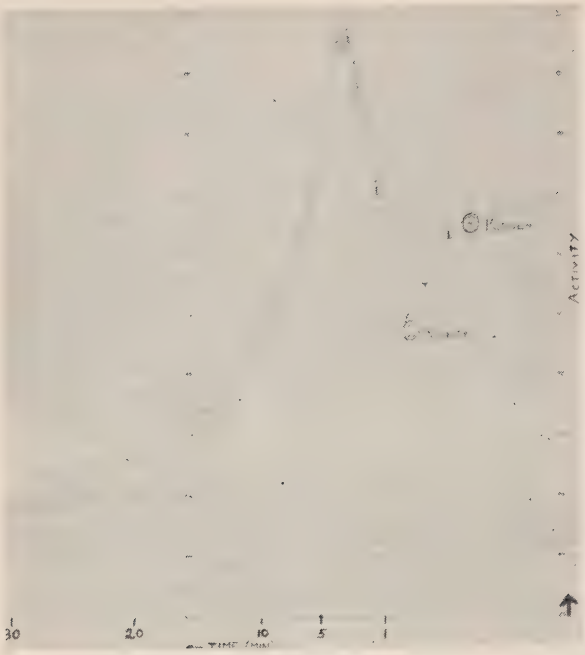


Fig. 1

than a minute commences within seconds after administration of the Hippuran® and is conventionally referred to as the "vascular segment." The shape of this segment is due in part to renal function since materials such as I^{131} albumin which are normally retained within the circulating blood produce a much flatter curve than is obtained using Hippuran®. Following this initial rapid spike, the curve continues to rise at a slower rate to form a second segment which normally reaches a peak within five minutes after isotope injection. This second or "functional" phase represents the rate of active tubular cell uptake and secretion of Hippuran® by the renal tubules. It is, therefore, the measure of the extraction efficiency of the kidney. This functional phase is superimposed on the radioactivity in the vascular bed of the kidney area. The final component of the renogram relates to the excretion of the Hippuran® from the kidneys. An example of an abnormal renogram of a patient being evaluated for hypertension is shown in figure 2. It may be noted that the renogram of the left kidney is essentially normal whereas that of the right kidney has a considerably different shape. There is a decreased rate of initial rise, a depression and delayed appearance of the peak, and a delay in excretion. This patttern is highly suggestive of renal artery stenosis which was subsequently verified by a selective arteriogram and then corrected surgically.

Figure 3 represents a renogram of a patient who had received 2 kidney transplants approximately two years previously. This patient has been followed with serial renograms since implantation of the kidneys. At the time of this renogram, there is evidence of slight depression of the functional peaks bilaterally and also a slight delay in excretion. This pattern is considered to be quite typical of a rather mild rejection reaction. This patient has demonstrated several such episodes at various times since the transplantation. By adjustment of medications, this rejection has been reversible; at the present time, the patient is doing well and leading a near normal life. A recent renogram of a 35-year-old patient who received a cadaver kidney following bilateral nephrectomy four months ago is shown in figure 4. The pattern is essentially normal and this patient continues to do well.

Another preparation receiving attention as evaluation of renal function is a diuretic labeled with radioactive mercury (Hg^{197} Neohydrin®). The shape of the curve is considerably different from that obtained using Hippuran® because of very slow clearance from the kidneys. Its slow

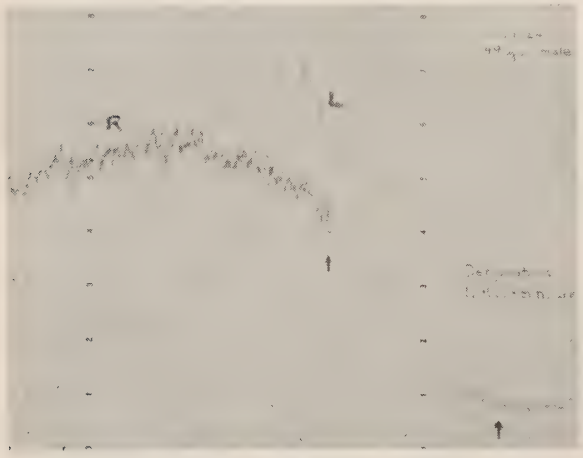


Fig. 2



Fig. 3



Fig. 4

clearance makes it an ideal agent for kidney scans. Figure 5 shows a scan of a pediatric patient with a small pelvic kidney on the right side. In these scanning studies, a scintillation probe is moved in a controlled manner over the area of interest. A focused collimator on the detector permits a point-to-point relationship to be established between the area being scanned and its recording. A gamma ray spectrometer permits selective reception of electric impulses produced by radiation coming from the target area while discriminating against those impulses resulting from background radiation. By means of a photo recorder, the impulses passing the spectrometer activate a light source which moves in parallel with the detector. This source exposes X-ray film as it moves. The intensity of the light and the frequency with which the light is turned on relate to the radioactivity as viewed by the scintillation detector.

Figures 6 and 7 represent scans made of an 18-year-old girl three months after she first noted difficulty in writing. Her symptoms progressed to a left hemiparesis at the time of hospital admission. Other physical findings of note were papilledema and hepatomegaly. The brain scan (Fig. 6) was performed with Hg^{197} Neohydrin® and showed increased activity in the right frontal area. This proved to be a large glioblastoma which could be only partially resected. A liver scan (Fig. 7) was performed with I^{131} rose bengal which clears through the parenchymal cells and may also be used to study liver function. This scan shows at least 3 large filling defects in the liver including essentially all of the inferior border of the palpable abdominal mass. A liver biopsy showed this to be a hepatoma. This has been our first demonstration of 2 primary neoplasms in 1 patient.

Recently, a new instrument has been added to our armamentarium for studying various body organs. This device is called a scintillation camera. It has no moving parts and functions in a manner quite analogous to an X-ray fluoroscope. Gamma ray photons passing through a collimating system strike a large crystal and produce scintillations which are viewed by a bank of phototubes. The signals from the phototubes are fed through a computer-analyzer system which determines the site of the origin of each scintillation and displays this as a flash of light on a cathode ray tube. The cathode ray tube may be

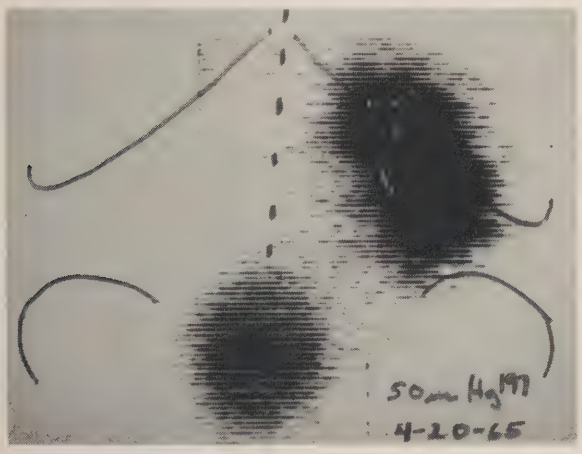


Fig. 5

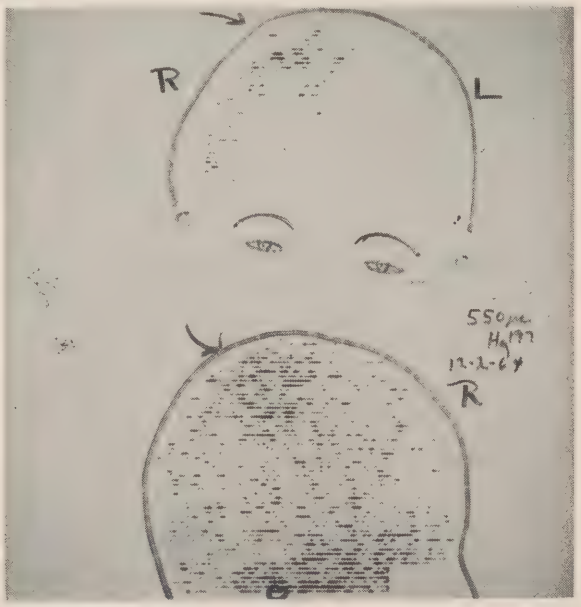


Fig. 6



Fig. 7

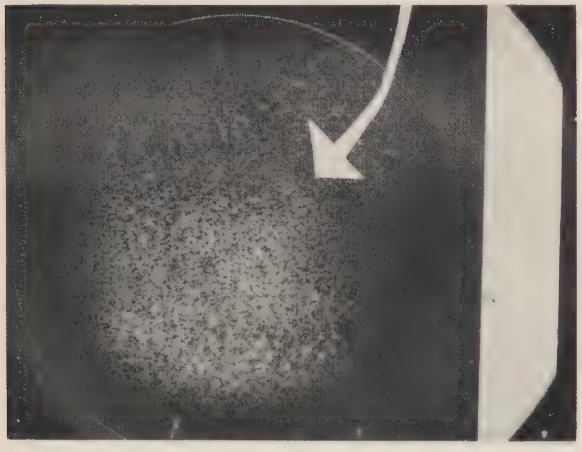


Fig. 8

viewed by a conventional camera or movie camera. This means that entire field of view which is 11 in. in diameter for the model in our clinic will be presented to the read-out device which at present is a Polaroid camera. Thus, radioactive materials with short lives can be used to distinct advantage. Larger doses of these radioactive materials may be administered to patients within limits of acceptable radiation exposure and information on transport or localization of these isotopes may be obtained relatively quickly.

At the present time, very few such radioactive preparations are available for our use. One of the few such materials is technetium-99m which is a decay product of molybdenum-99. The radioactive molybdenum-99 is supplied to us on a resin column from which we may elute the radioactive technetium for various studies. Thus far, we have studied the localization of radioactive technetium as the pertechnetate ion in brain tumors, salivary glands, and the stomach. We are also attempting to tag the technetium to albumin to permit a colloid to be formed which might then be used in liver and spleen studies, as well as for visualization of the lung. Figures 7 and 8 illustrate Polaroid pictures taken using the scintillation camera and demonstrate brain pathology. Figure 7 shows a left lateral projection on a patient who was admitted for evaluation of headache and recent onset of seizures. This picture was obtained two hours after administration of technetium-99m. The entire head is visualized with highest activity seen in the salivary glands and saliva in the mouth. The arrow points to the lesion which at surgery proved to be a large glioblastoma with a necrotic center. Figure 8 illustrates a lateral projection on a patient who was hospitalized on the psychiatry service because of personality changes. This study was performed with Hg^{197} Neohydrin® so that orientation is more difficult. The lesion lies in the left temporal area as seen by the arrow. This patient had a history of chronic mastoiditis and at surgery an abscess was found and drained.

SUMMARY

The examples shown in the previous paragraphs are but a small part of nuclear medicine today. There can be no doubt that tests such as these can be of definite value in diagnosis of various diseases. In all cases, careful attention must be paid to the technical aspects of the test so that reliable results may be obtained. Careful consideration must also be given to radiation exposure of patients. It is, therefore, our approach in nuclear medicine to develop procedures which can be performed simply, are reliable, and may be done with a minimum of radiation exposure. With attention to these details, we are confident that nuclear medicine will continue to grow and play an increasingly important role in the medical evaluation of our patients.

Supported by grants from the U.S. Public Health Service (project No. HE 06314), the Graduate School, University of Minnesota, and the American Cancer Society (Institutional Grant)

The Ataxic Patient

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Ataxia is an impairment of coordination of muscle function, produced either by lesions of the cerebellar tracts or hemispheres, or by lesions of the posterior columns. The incoordination is manifested chiefly in the lower limbs by gait disturbance and may result from a wide range of conditions affecting different age groups.

Ataxia and incoordination are tested by requiring a patient to perform complex motor functions such as: the finger-to-nose test, the finger pursuit, check and rebound, testing for intention tremor, performing rapidly alternating movements of the hands, doing tandem walking and tandem standing, hopping on one foot, or rapidly changing direction while walking. Inability to perform the above motor functions normally suggests that incoordination is present and due to cerebellar deficit.

INFANCY

1. *Birth anomalies.* Ataxia in this age is rare and one of the more common causes is anomalies of the central nervous system. Agenesis of the cerebellum becomes apparent as the child begins to grasp objects. It is then that intention tremor and awkwardness are noticed for the first time. The patient generally has a congenital nystagmus which is obvious when the child's eyes look to either side. Agenesis of the cerebellum produces an impairment of ability to sit or stand without losing balance. Consequently, learning to sit, stand, and walk is delayed. Neurological examination shows sparing of the pyramidal system.

Treatment is directed towards training the child to function within the limitation of the deficient brain. Gait training may be prolonged but independent gait is frequently possible.

2. *Birth trauma (cerebral palsy).* Prenatal or natal trauma of mechanical or infectious type can focally destroy the coordinating centers of the central nervous system. This condition usually has associated diffuse central nervous system damage manifested by mental deficiency, athetosis, and spastic diplegia. Historical data are necessary to confirm the diagnosis; however, the diffuseness of the deficit and a stationary or improving course may at times be the only substantiation of this diagnosis.

CHILDHOOD

1. *Chicken pox encephalitis.* In this age group chicken pox is the most common cause of acute ataxia in a previously normal child. A febrile illness with vesicular rash and a history of exposure to the disease confirm the diagnosis. The severity of the central nervous system deficit may show no relationship to the severity of the systemic infection. The deficit usually progresses for three weeks and then improves. The prognosis for complete recovery is good. No prophylactic measures are available for chicken pox at this time, nor can one alleviate or modify the encephalitis process. Therapy is directed toward retraining the child if any residual deficits occur.

2. *Drugs.* Accidental, intentional, or medicinal administration of barbituates, diphenylhydantoin (Dilantin®), and tranquilizers are a common cause of acute ataxia in this age. These drugs have an associated sedating effect which suggests the syndrome of inebriation and the patient frequently complains of vertigo and nausea. These intoxications are self-limiting and remiss spontaneously in days providing the drug is discontinued. Generally, no residual deficit is seen.

3. *Friedreich's ataxia.* This condition is hereditary and is transmitted as a mendelian recessive, tending to affect several brothers and sisters of a given family. The onset of this disorder is slowly progressive, beginning between the ages of 5 and 10 years. The primary manifestation is that of ataxic gait; however, lateral column involvement may be prominent producing a spastic diplegia. These patients frequently have associated skeletal deformities such as pes cavus, dorsal kypho-

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scoliosis, and a cardiomyopathy. Neurological examination reveals severe ataxia, nystagmus, dysarthria, unsteadiness of head, and usually slight incoordination of the upper extremities.

Treatment is directed towards permitting maximum utilization of the remaining functions by rehabilitation. This condition may arrest spontaneously or may progress to complete disablement of the patient.

4. *Tumors of the cerebellum.* In this age range, usually under 10 years, primary gliomas such as astrocytoma, ependymoma, and medulloblastoma of the cerebellum occur. These tumors produce a rapidly progressive ataxia with gross gait disturbance. The most malignant of the group, the medulloblastoma, shows a predilection for the male child. Tumors of the posterior fossa produce signs of increased intracranial pressure early which manifests as headache, loss of visual acuity, inattention, irritability, and somnolence.

Therapy is surgical. The cystic astrocytoma may be successfully removed in some cases giving the child many years of near-normal life. The ependymoma is less amendable to surgery being located near the vital structures of the brainstem. Medulloblastomas are aggravated and seeded by surgical manipulation, the treatment of choice in this case is radiation.

ADULT

1. *Multiple sclerosis.* This is the most common cause of ataxia in the young adult. A careful history usually reveals previous transient neurological complaints such as diplopia, visual disturbances, hemiparesis, or paresthesia. The neurological examination usually shows scattered neurological deficits, such as bilateral positive toe signs, reflex alterations, nystagmus, scotomata, or incoordination. The presence of recurrent deficits with scattered neurological finding in a young patient with ataxia characterizes this disease.

There is no specific treatment for this disease. The acute exacerbations frequently respond to intravenous adrenocorticotrophic hormone (ACTH). During periods of remissions, these patients may be treated expectantly with vitamin supplements, crude liver extracts, intramuscular ACTH, and forms of nicotinic acid (Nemase® or Roniacol®) in hopes of deterring an exacerbation. General hygenic measure should also be stressed. Chilling, fatigue, pregnancy, and toxic exposure to alcohol should be avoided. During periods of infections, the patient needs early intensive medical care, increased rest, and antibiotics.

2. *Alcohol.* This is a most common cause of transient ataxia and may at times cause a persisting ataxia in this age group. The diagnosis of alcoholism in the acute stage is aided by the aroma of liquor, the inebriated behavior with its sedated injudiciousness, and by its remitting course. The chronic alcoholic ataxia, which is often confused with parenchymatous cerebellar degeneration, is diagnosed by associated signs. Liver dysfunction with bleeding tendencies and spider nevi are present in the alcoholic, as is tremulousness of the hands and lips and poor oral and body hygiene. Associated neurological signs of peripheral neuritis manifesting motor weakness of the legs and hyperesthesia of the soles of the feet are consistently present. Oculomotor imbalance may also occur in this disorder which is then termed "Wernicke's Syndrome."

Treatment is abstinence from liquor and beer, administration of therapeutic levels of parenteral vitamins, and permitting the brain tissue to compensate for its dysfunction. Prognosis for the incoordination is much poorer than for neuritis, encephalopathy, or oculomotor deficits.

3. *Dilantin®.* This age group contains many individuals (two people out of every 100 have a convulsive disorder) who take anticonvulsants, usually Dilantin® and a barbituate. Dilantin® toxicity should be suspected wherever there is a history of seizures, where classical hypertrophy of gums is seen or where a patient with acneform rash shows recent development of ataxia.

Treatment for this condition consists only of withdrawal of medications. The ataxia may require weeks or even months before it completely disappears. Rarely permanent ataxia persists.

4. *Cerebellar tumors.* Primary tumors of the cerebellum develop in this age group. The malignant medulloblastoma does not occur in adult life. Astrocytomas, ependymomas, and the midline angioblastoma are seen in adult life. These tumors produce slowly progressive ataxia which develops over months or years. Posterior fossa tumors produce increased intracranial pressure relatively early causing headache, visual disturbances, impaired mentation, and somnolence. The treatment is removal of tumor mass, if possible, surgical relief of spinal fluid block, and irradiation of the suspected site of origin.

5. *Acoustic neuroma.* Paroxysmal bouts of vertigo associated with tinnitus and slowly developing deafness are common in this lesion. However, in some patients these symptoms may be minimal and the chief complaint is that of increasing incoordination. Neurological examinations frequently show a loss of the corneal reflex on the side of the tumor, a loss of vestibular response when caloric testing is performed on the side of the tumor, and subtle or profound ataxia

on the side of the acoustic neuroma. Laboratory tests frequently reveal increased protein in the cerebrospinal fluid. X-ray of the internal auditory meatus at the site of the lesion will frequently show erosion. This tumor has a very slow course, usually given in terms of years.

Treatment, when the tumor is small, is surgical removal. If the lesion is permitted to grow to a large size, it is mechanically impossible to remove without damaging vital brainstem centers.

6. *Thrombosis of the posterior inferior cerebellar artery.* In this age range the development of sudden severe vertigo which causes the patient to fall to the ground following which ataxia persists is the classical "Wallenberg Syndrome." The neurological examination in these cases reveals loss of facial sensibility on the lesion; the opposite side of the body may be less sensitive to touch and pain than normal. Cranial nerves 9 and 10 may be affected on the side of the lesion, manifested by decreased gag reflex ipsilaterally.

Prognosis is generally good and with bedrest most patients slowly recover. The ataxia is the most disabling sign requiring the longest time for improvement. Patients also may have diabetes mellitus which must be diagnosed and treated.

7. *Spinal cerebellar ataxia of Marie.* Familial spinal cerebellar degenerations which occur between the ages of 20 and 40 years have been termed Marie's Cerebellar Ataxia, a slowly progressive gait disturbance associated with dysarthria and mild upper extremity incoordination.

MIDDLE AGE

1. *Tabes dorsalis.* Tabetic involvement which occurs in this age range is characterized by slowly progressive ataxia. Historical data concerning the initial infection is of great diagnostic aid when available. Specific complaints such as "lightening pain," a sensation of sharp, "jabbing" discomfort, localized to an area the size of a quarter for a period of one to several days, which then remisses only to recur at another site for a similar period of time, are highly suggestive of this diagnosis. Pupillary abnormalities such as irregularity, asymmetry in size, and impaired light response, strongly suggest the luetic infection. Charcot joints and gross bony destruction of the knee joint are characteristic of dorsal column destruction from a luetic infection. Tabes destroys bladder function early with resultant urinary dribbling.

The treatment of tabes is one million units of penicillin daily, intramuscularly, for twenty consecutive days; if the progress of the neurological deficit is not rendered stationary or improving, a repeat course of therapy is indicated at three-month intervals until progression is stopped. Fever therapy and penicillin may be given.

2. *Subacute combined degeneration.* Pernicious anemia and malabsorption syndrome with combined system disease occur commonly in this age group and manifests as ataxia. This gait disturbance is produced by a degeneration of the posterior columns. Neurological examination reveals an inability to acknowledge the position of the toes when hidden from view; there is an inability to feel the vibration of a tuning fork (C 128) when it is activated and held firmly against their shinbone. Compression of the Achilles tendon and the calf muscles by pinching does not cause the patient pain. Examination of these patients frequently reveals a "stocking-like" loss of pain and touch appreciation in the feet. The toe signs are often positive. The neurological deficits may or may not be associated with an anemia, but there is always a positive Schilling test response to B_{12} and an achlorhydria even with histamine stimulation.

Treatment for this condition consists of intramuscular vitamin B_{12}, 1,000 μg. weekly with an intramuscular crude liver extract of 2 units per cubic centimeters, given 2 cc. weekly until maximum improvement is obtained. A supportive injection of each, monthly, for life is required.

3. *Parenchymatous cerebellar degeneration.* In individuals 55 years and older, the gradual development of ataxia with no other signs of central nervous system involvement occasionally occurs. The course is insidious with spread to involve upper extremities and to produce dysarthria very late in the course. Etiology is undetermined and no therapy is available.

OLD AGE

1. *Cerebellar hemorrhage.* Patients in this age range who have relatively severe hypertension occasionally devolp sudden cerebellar deficit of classical stroke variety. The initial symptomatology is occasionally associated with severe vertigo and headche. After the insult, the condition rapidly becomes stationary and then improves. The ataxia is unilateral and involves both the arm and leg. There is no specific therapy.

2. *Degeneration of the posterior columns.* In senescence, the gradual loss of posterior column function for undetermined reasons does occur and produces subtle progressive ataxia for which we presently have no therapy.

Carcinoma Arising in a Congenital Lung Cyst

Report of a Case

B. E. KONWALER, M.D., and LEROY HYDE, M.D.

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MAIER[1] HAS pointed out that the use of the term "pulmonary cyst" without qualification is rather unsatisfactory. Consequently, cases of carcinomatous change within pulmonary cysts have included cases in which the carcinoma developed in a bronchiectatic cavity and cases in which bronchogenic carcinomas have become cystic. The development of bronchogenic carcinoma in a true congenital bronchogenic cyst is not a frequent occurrence. A number of papers have appeared in which the actual identification of the mechanics of the cystic formation and the structural characteristics of the cyst wall have not actually been determined. Thus, Korol[2] reported 45 cases of congenital cystic emphysema in which carcinoma was encountered as an incidental finding and concludes that the incidence of lung cancer is significantly greater in cases of congenital cystic emphysema than in the general population. However, in review one finds that most, if not all, of his cases fail to meet the criteria for a congenital cyst. In some cases, for example, diagnosis was made by means of a biopsy of a lymph node which showed anaplastic carcinoma. In another case no biopsy is included but the author assumes that the case is a bronchogenic carcinoma developing in a cyst since an obstructive lesion was found in the right upper lobe bronchus. Bauer[3] similarly has pointed out that very few cases of actual bronchogenic cysts in which carcinoma develops have been reported and states, "If one accepts the criticism offered by some authors, there are only 3 cases in English literature in which there is irrefutable documentation of a carcinoma arising in the wall of a congenital pulmonary cyst." Bauer's case, from his photomicrographs and gross appearance, is almost identical to the case which we are herewith reporting. A similar case has been reported by Huntington in 1963.[4]

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CASE REPORT

A 42-year-old pharmacist came to the hospital on March 6, 1962, because of malaise and vague chest ache. Past history revealed pneumonia of the left lung with subsequent development of "a lung abscess" at the age of 13. This was allegedly drained through the bronchial tree and he was told on several occasions that he had a "lung cyst." The man was a heavy smoker and admitted to smoking at least 1 pack per day since about 17 years of age. In 1941 he enlisted in the Navy and apparently was considered physically fit for duty. In 1944, while on active duty in the Phillippines, he noted a small hemoptysis, was hospitalized in the Naval Hospital, and was told that he had a cavity in the left midlung field. Various skin tests and sputum examinations were all negative. He had difficulty in February 1962 when he again had a small hemoptysis. He saw his physician at this time who noted the lung cyst in the left midlung field. The patient continued to work during all of this time.

Physical examination on the first admission was entirely within normal limits. The patient was well developed, well nourished, and weighed 125 lb. Blood pressure was 120 mm. systolic and 70 mm. diastolic.

The patient was entirely asymptomatic during his short hospital stay. Previous X-rays were obtained and chest X-rays of December 1941, October 1944, and March 1962 were similar, revealing a thin-walled lucency in the left midlung field which measured 7 cm. in diameter (Fig. 1). The intermediate purified protein derivative skin test was positive, and the coccidiodin 1 to 100 and histoplasmin 1 to 100 skin tests were negative. The bronchoscopy was entirely normal. Four sputum cultures were negative for tubercle bacilli and 4 sputum cultures were negative for fungi. Routine laboratory work was noncontributory. Since the patient was entirely asymptomatic, and since the left lung cyst was known to have been present for at least twenty-five years, it was felt that no therapy was indicated and he was discharged on March 26, 1962.

Several weeks following discharge from the hospital he noticed vague pain in the left posterior chest. This was at first easily controlled by aspirin but subsequently required codeine. He coughed slightly and produced about 5 cc. of mucoid sputum daily, rarely with small flecks of blood. The patient was readmitted to the hospital because of the left posterior chest pain on May 2, 1962.

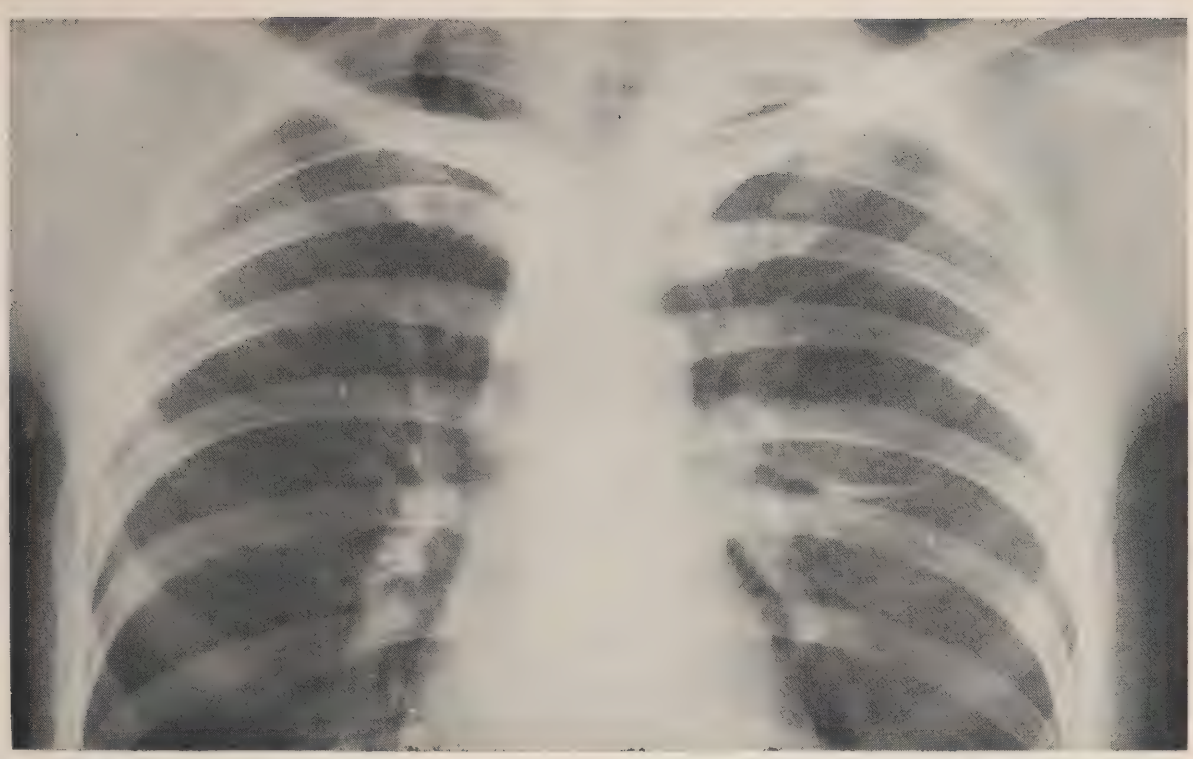


Fig. 1. Chest roentgenograms between December 1941 and March 1962 were unchanged and revealed large cyst in left upper lobe noted on this film of March 6, 1962.

During the second admission, fluid in the lung cyst was noted for the first time and planigrams revealed a small nodule medial to the cyst. Numerous sputa were negative for tumor cells and repeat bronchoscopy on May 29, 1962, was within normal limits, except for very minimal mucoid secretions from the superior segment of the left lower lobe. Bronchial aspirate was negative for tumor cells.

Hemoglobin was 13.8 gm. percent and hematocrit was 42 percent. The white blood count was 9,900 with 67 percent neutrophils, 23 percent lymphocytes, 5 percent monocytes, and 5 percent eosinophils. The erythrocyte sedimentation rate was 37 mm. in one hour. The patient was again discharged on June 5, 1962.

The patient was readmitted on July 17, 1962, because of persistent pain in the left posterior chest. Because of the nodule noted on X-ray on the medial wall of the lung cyst, it was decided to perform a left thoracotomy.

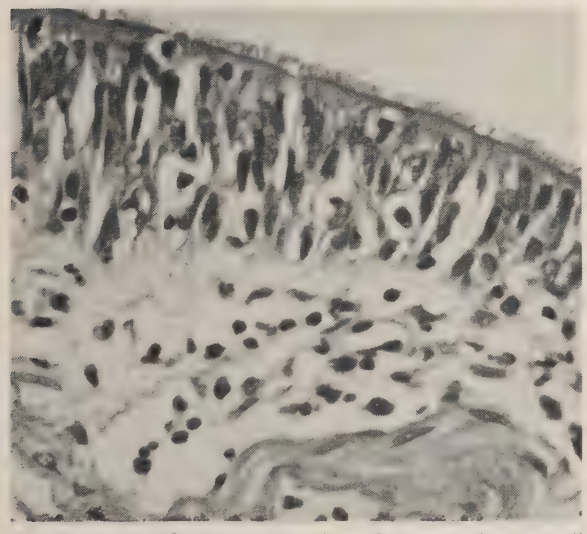


Fig. 2. Section from superior, lateral aspect of cyst wall ($\times$ 715) showing ciliated pseudostratified epithelium in upper half and some smooth muscle in lower half. Epithelium appears normal.

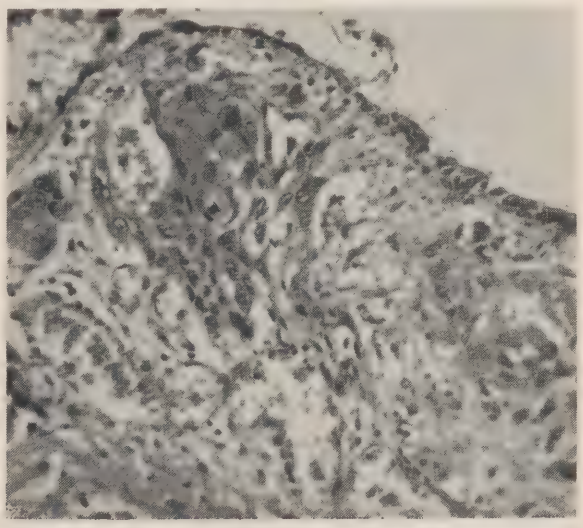


Fig. 3. Section of medial and lower segment of cyst wall showing loss of cilia, flattening of epithelium, desquamation of epithelium, and invasive squamous-cell carcinoma, $\times$ 300.

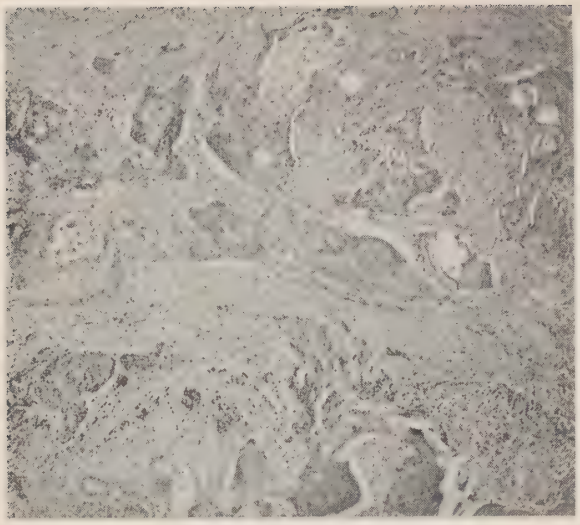


Fig. 4. Section of deeper portion of medial and lower portion of cyst wall showing extensive invasive carcinoma with epidermoid features, × 65

At surgery, the cyst was found adherent to the posterior and lateral chest wall. A biopsy from the lateral upper portion of the cyst failed to reveal malignancy. A segmental resection was performed to include the entire cyst and a segment of lung surrounding it. When microscopic sections were made from the medial wall, infiltrating squamous-cell carcinoma was found. Following the segmental resection, the patient received radiation therapy but succumbed to the malignancy on Feb. 1, 1963, with metastases to the mediastinal and mesenteric lymph nodes.

DISCUSSION

From a study of the microscopic sections, the cyst showed histological findings consistent with congenital lung cyst and was lined on the superior and lateral wall by pseudostratified columnar ciliated epithelium (Fig. 2). Medially, however, the epithelium showed a transition to nonciliated, atypical cells which desquamated readily and showed malignant invasive capabilities (Figs. 3 and 4).

In an extensive necropsy study, similar changes in the bronchial epithelium have been described by Auerbach and Stout[5] in heavy smokers. Since this patient's cyst at times contained fluid in its dependent portions, and can thus be assumed to have communicated with a bronchus, one (B.E.K.) of the authors speculates as to whether the possible carcinogens presumed to be present in smoke may have been more concentrated in the dependent portions containing fluid where the invasive carcinoma was found, while not involving the superior portions due to less concentration.

SUMMARY

A case of bronchogenic carcinoma developing in a congenital cyst is reported. One of the authors (B.E.K.) believes that the use of cigarettes in the amount stated (more than 1 pack per day for twenty-five years) resulted in the concentration of carcinogens in the dependent portion of the cyst where fluid had accumulated. However, the second author (L.H.) feels that smoking is not related to carcinoma in this cyst.

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DROP ATTACKS appear to be a diagnostic symptom of intermittent vertebrobasilar insufficiency. Attacks bring sudden loss of strength in the legs and collapse but do not affect hearing, sight, or speech; however, persons with akinetic seizures generally suffer altered consciousness. Frequency of the attacks varies with different individuals. Although the exact pathogenesis is unknown, transient ischemia of the lower portion of the brainstem most likely is the cause. Conditions that are known to bring on focal cerebral ischemia include orthostatic hypotension, compression of the extracranial portion of the vertebral artery, and cervical spondylosis. Management of the attacks is aimed at relieving the source of focal cerebral ischemia. If lesions cannot be corrected surgically, a cervical collar, correction of postural hypotension, or anticoagulant therapy should be considered.

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Metastatic Granulosa-Cell Tumor of the Lungs

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AN UNUSUAL CASE of metastatic tumors of the lungs was recently seen in our practice.

CASE REPORT

A 61-year-old female was admitted to the hospital with complaints of pain in the chest, not related to the respiratory movements. She had dyspnea, was coughing, and produced some sputum. Once, the sputum was hemorrhagic. Two years before, a myoma of the uterus together with the ovaries was removed in another hospital with a total weight of 8,900 gm.

Bodily examination did expect extensive infiltration or fluid in the pleural space. The weight of the patient was 72.5 kg. and the blood pressure was 145/90 mm. Hg. Blood sedimentation rate: 22 mm. after one hour. Hemoglobin: 14.1 gm. per 100 ml. Leucocytes: 9,200 per cubic millimeters. Blood smear differentiation: 0-4-2-71-20-3

The X-ray film (Fig. 1) showed a density of the major part of the right lung due to fluid, and in the left lung a circumscribed density against the lateral chest wall.

Through pleural puncture, 800 ml. of hemorrhagic fluid was removed. The X-ray film (Fig. 2) showed circumscribed densities in the right lung. The whole clinical picture was clearly suspect for multiple metastatic pulmonary tumors.

Careful cytological examination of the sputum showed no signs of malignancy. In the thoracic fluid, however, malignant cells were found. These cells with folliculoid structure were highly characteristic, so the diagnosis "metastatic granulosacell tumor" was made.

After these findings it was necessary to review the original microscopic slides of the ovaries, removed two years before. In one of these slides, Dr. Porton found a clear, circumscribed, luteinized, granulosa-cell tumor with all signs of malignancy. Folliculoid structures were found (Call-Exner bodies) with cell arrangements resembling a rosette. Lymph node biopsy after Daniels showed no signs of metastatic tumor growth.

Through puncture of one of the pulmonary lesions, some small fragments of tissue could be obtained, which microscopically confirmed the diagnosis.

The typical arrangements of cells was seen, as well as the marked resemblance of some of the structures suggesting embryonic organ development in some malignant teratomas. Also, myxoid



Fig. 1. X-ray film at admission to the hospital showing density of the major part of the right lung due to fluid and a circumscribed density in the lower part of the left lung

areas with spindle cells and stellate cells were found.

In smears from bone marrow from the sternum, some "atypical, probably pathological" cells were found but could not be identified as tumor cells. A smear from the vagina showed (para) basal cells with some precornified epithelium cells; no signs of estrogenic activity could be found.

The patient was allowed to go home for some

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Fig. 2. X-ray film after removal of 800 ml. hemorrhagic fluid from the right thoracic cavity. In the right lung are multiple circumscribed densities.

weeks and unfortunately died suddenly. Postmortem investigations were impossible.

DISCUSSION

Pulmonary metastatic granulosa-cell tumor is seldom reported in literature and seems to be an extremely rare event. The *Tumor Atlas of Pathology* gives no example of this metastatic tumor. Only a small number of granulosa-cell tumors are malignant and most of these demonstrate their malignancy within the abdominal cavity.

In literature, only 1 previous report could be found; Rigler[1] in 1952 reported a case very similar to ours in a woman of 51 years.

In general, metastatic granulosa-cell tumors are characterized by the generally undifferentiated aspect of the tumor, except for denser concentrations of cells in some areas. There are features identical to malignant teratomas of the mediastinum, as reported by Schlumberger[2] in 1946.

SUMMARY

A case of multiple metastatic granulosa-cell tumor in a female of 61 years is reported. Diagnosis was made through cytological examination of thoracic fluid and biopsy of one of the pulmonary lesions.

Confirmation could be obtained by carefull reexamination of the microscopic slides of the ovaries removed two years before. In one of the ovaries the primary tumor was found.

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HYPOPLASTIC ANEMIA was diagnosed in a 7-year-old girl. During the next two and a half years, treatment included splenectomy; prednisone, stanozolol (Winstrol®), and testosterone propionate; and 67 transfusions of whole blood and 4 of platelets. The patient continued to be anemic, and leukocyte and platelet counts were consistently depressed. Since other treatment had failed, bone marrow from the patient's identical twin sister was infused. The patient was greatly improved six weeks after transplantation: Hemoglobin was 12.1 gm.; leukocyte count, 8,000; and platelets, 261,000 per cubic millimeter. The marrow showed active granulopoiesis and erythropoiesis and contained adequate megakaryocytes for the first time. The patient has continued to do well without further blood transfusions.

STEPHEN D. MILLS, M.D., ROBERT A. KYLE, M.D., GEORGE A. HALLENBECK, M.D., GERTRUDE. L. PEASE, M.D., and IAN C. CREE, M.B., Mayo Clinic and Foundation, Rochester, Minn. Bone-marrow transport in an identical twin. J. Amer. med. Ass. 188:1037-1040, 1964.

A History of Radiology in Montana

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THE RECORDS regarding the early use of X-rays in Montana are sketchy and incomplete.

One of the first men to use X-ray was Dr. S. W. Menshall. He moved from Philipsburg to Missoula in 1899 and was a specialist in Eye, Ear, Nose, and Throat. He used X-rays for diagnosis.

Dr. F. W. Spelman, who located in Anaconda in 1890, was later on known as an expert in the use of X-rays. Other men who were known to use X-rays in the late 1890s were E. A. Crane, Missoula, and D. W. McKay, White Sulphur Springs. Dr. McKay was known as one of the first to use X-rays for diagnosis in Montana.

The equipment used by these pioneers was what was known as an X-ray attachment to a static generator. The static generator produced the necessary high voltage to energize the tubes. However, the machines were cranky and required a great deal of adjusting in order to produce satisfactory plates. The usual method of testing to determine whether the desired conditions to operate were attained, was to place the hand behind a fluoroscope screen. Many early operators received injuries in this way that eventually caused their deaths.

Dr. C. F. Watkins was one of the first men to use X-rays in this part of the country. His widow still lives in Billings, and I had a very interesting conversation with her recently. Dr. Watkins graduated as an M.D. from the University of Michigan in 1901. He spent some time at the Northern Pacific Hospital in Brainerd, Minn. Then he went to Missoula. While in Missoula, according to his wife, he found an old X-ray machine in the basement of the hospital. He reassembled it and was able to use it effectively. I knew Dr. Watkins well. He was one of the men who used his hand to test his fluoroscope. He received injuries to his left hand which finally resulted in carcinoma. His arm was amputated, but the cancer spread and eventually caused his death. He noticed a redness of his hand in 1906 and recognized that this was due to X-ray. At that time he had been using X-rays for at least three or four years. He continued to practice, but he was forced to give up surgery in 1926. He did acquire some radium at this time and did some very effective work with radium. The left arm was amputated in the Crile Clinic in 1934. He lived approximately two or three years longer and died in March 1936 at the age of 63.

Another man whom I knew well was Dr. Lyle Haverfield, who lived in Hardin. He, too, used his hand to test his fluoroscope and did fluoroscopy with a tube without any shielding. His course was somewhat similar to that of Dr. Watkins'. He eventually had several operations and died from the effects of radiation cancer of the skin of his hands.

Another friend of mine was Dr. Adams of Red Lodge, who had very serious lesions on his hands. His were due to exposure during fluoroscopy. He had several minor amputations but died of other causes.

Radiology in Montana has grown to an extent beyond anything I thought probable in the 1920s. In 1925 John H. Bridenbaugh, M.D., was the only radiologist in Montana who was a member of the national societies. Today we have at least 19 qualified radiologists in the state. They are very important members of the clinic and hospital staffs. I am sure that radiology is making an excellent contribution to the practice of medicine in Montana.

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Herman Oscar McPheeters, M.D.

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IN MY LIBRARY I have a book written in 1869 by Dr. Elijah B. Hammach. "The Family Physician" was in no respect written for the medical profession but, on the contrary, against the doctors of his time. In paging through this monologue I came on the following statement: "I have cured some very old and obstinate ulcers by warm water dressing and bandages commencing at the toes and bandaging them to the knee and painting them occasionally with the solution of nitrate of silver." The relationship to stasis and the leg ulcers was not well understood at that time but the seed for the study of the cause and treatment must have been already sown.

Great strides have been made in the past ninety-odd years since that statement was made. Ulcerations of the lower extremities are now known to be caused, or at least aggravated, by the presence of varicose veins. The function of the veins has been studied and much of it understood. The pathology of the venous system has been the subject of much research, and although the reparative procedures on nonfunctioning veins is still in its infancy, the surgical treatment for the eradication of unsightly, painful, and dangerous varicosities has been developed to a high degree.

Many procedures have been devised, revised, rejected, and a few reexamined in a new light. Basic principles remain. These principles have been painstakingly developed in hospitals and laboratories throughout the world. Much of the development of adequate therapy has taken place in the past twenty-five years. Many investigators must be given credit for the present day status of venous therapy. During this period there have been a few who have been outstanding in their contribution to the understanding of this disease. One of the men who has given so much is the subject of this paper.

Herman Oscar McPheeters was born on Jan. 31, 1891, in Mankato, Minnesota. His father was born in Indiana, of Scotch and Holland-Dutch ancestry. His mother was born in Indiana and was of English-Welsh origin. His parents met at Prior Lake, Minnesota, which was then called Seven Corners, while both were teachers there. Later they moved to Mankato. They lived there at the time of the Sioux uprising, and farmed during the time of the frontier Indian wars.

When Herman Oscar was 6 years old, the family moved to Hill City, Minnesota, where they became farmers. The McPheeters family was the second family to settle in this area. The first few years of living here were similar to frontier days; mail was picked up about 3 times in the summer but more often in winter because travel was easier on sleds and the farm chores were less. The reason for this was that mail was picked up from Aitkin, which was 42 miles away. This town was also the source of all supplies for the homesteaders.

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During his school years at Hay Point, Herman had an advantage (or disadvantage) over the other students because the teacher, a graduate of Hamline University, took his room and board at the McPheeters' household. This relationship had a bearing on his choice of college, and indirectly on the course of his entire career. During the years at Hay Point, he worked on the farm with his father.

After graduating from country school, he entered high school at Aitkin. He worked his way through school by doing janitorial work and hauling wood for the school furnace. During his senior year Herman and 4 other boys rented a house in Aitkin. They called it Bakeline Hall. Together they were able to make ends meet, at a cost of $2.50 per week per student. Each boy had his own chores to do; some did the cooking and others kept the house in order.

It was while he was in high school that his eldest sister became ill with tuberculosis and was hospitalized at Brainerd. He visited her regularly and during these visits became acquainted with the doctors. These men were instrumental in his becoming interested in the study of medicine. He decided then to go on to college and medical school.

In 1909 he graduated from high school and received a scholarship. This scholarship was for either Hamline or Carleton College. Because his grade school teacher was a graduate of Hamline University, he decided to take his training at that school. During his college years he became an exceptional athlete and distinguished himself in football, basketball, and track. He received a letter in each of these sports. In 1911 he was named All-State Center and captain of his team.

Personalities played a large part in Dr. McPheeters' career. He chose Northwestern University Medical School, which he entered in 1911, because he was well acquainted with Charles Pierce, who was team captain at Hamline when Dr. McPheeters played on the football team. Charles Pierce later opened a medical practice in Wadena, Minnesota. During the first two years at Northwestern, in addition to his regular medical studies, he played center for the football team. While at the university, he pledged Nu Sigma fraternity. He graduated from Northwestern in 1915, and interned at Wesley Memorial Hospital in Chicago.

In 1917 he began the practice of medicine in Genoa, Illinois. Again destiny intervened. One of the surgeons in the hometown of Mrs. McPheeters died suddenly and the town was left in need of another physician. Because of the necessity of having a general practice physician in the area, he left Genoa and opened an office in Redwood Falls, Minnesota. His established practice began to increase but again fate changed his plans. World War I began and he entered the military service. He was inducted at Fort Snelling, Minnesota, and entered as a First Lieutenant in April, 1918. His first assignment was to Replacement Hospital A. He went to France with this unit. His assignment in the hospital was on the casualty operating team. After serving in Paris and the field, he was reassigned to Mobile Hospital No. 7. In this unit, his primary task was that of procurement of supplies.

On his return to the United States in 1919, he thought very seriously of accepting a fellowship in surgery at the Mayo Clinic. Friends, however, persuaded him to give up the idea; as he says, "way into the wee hours of the morning they talked to me and eventually I changed my mind." He then entered general practice in Minneapolis and opened his office at Chicago and Lake Street.

He remained in practice at this location for six months and then accepted a position with Dr. N. H. Sheldrup, a surgeon with whom he remained for six years. This was invaluable training for him. Dr. Sheldrup and his team of assistants, would do 6 to 8 major surgical procedures a day. Consequently, in six years most of the then-known surgical operations were performed many times. In 1924 Dr. McPheeters left group practice and began private practice in the Physician and Surgeon's Building in Minneapolis. He is still located in this building. It was in the next few years that he became interested in varicose veins.

Dr. McPheeters began to realize that patients who were suffering from varicose veins, and its complications, were not given adequate treatment. Frankly, during this period in medicine, the varicose vein patient was practically not treated at all. He had the insight to believe that something could be done to help them. This realization, plus his enthusiasm and great energy, were probably responsible for the beginning of varicose vein therapy in this area.

In 1928 he organized and staffed the varicose vein and ulcer clinic at the Minneapolis General Hospital. Stasis ulcers were the main problem in the clinic. It was here that he began to develop his ideas of supportive treatment with the Unna boot and elastic bandages. It was during this time that he began to formulate his theory of the "venous heart" with the sponge therapy. Because of the great number of complications that followed the various surgical procedures at the time, he became the protagonist for the injection treatment of varicose veins. This was a position

which he changed as he developed and formalized an adequate treatment for varicosities. Dr. McPheeters probably promulgated more forcibly than any other author at that time the fact that stasis ulcers and varicose veins were related. He also showed by X-ray techniques the direction the flow of blood would take in large varicosities and demonstrated the existence of incompetent communicating veins.

As his technique progressed, he began to realize that something other than local injection treatment needed to be done to further insure the permanent eradication of the varicosities. He then consulted Dr. John Homans in Boston and Dr. Matas in New Orleans. They were considered to be the best authorities on the venous system at that time. They convinced him that a high ligation was necessary and that this method, combined with the retrograde injection of sclerosing material probably would be preferred to local injections. This is the type of treatment that he used for many years, developing it to a great advantage in the treatment of varicosities. The idea of retrograde injection served for the development of "empty vein technique" which is still today the most effective method used to obliterate a large segment of a varicose vein with sclerosing material. In 1946 the surgical treatment of varicose veins was completely revised with the publication of a paper by Robert Linton of Boston, advocating intraluminal stripping of varicose veins combined with adequate ligation. Dr. McPheeters was not convinced at first, most probably because of the success that he had with the ligation and the retrograde injection therapy. The desire to give the best of himself to his patients, however, led him to inquire more about the process. During this time he visited Veterans Hospital in Minneapolis where the stripping procedure was being developed and used. The thoroughness with which he investigated everything he did prompted him not only to take the advice of the local medical circles but to get to the source of the problem. In 1949 he went to Boston to see Dr. Linton and was convinced that ligation plus stripping of the varicosities was a superior method. He returned from the East with enthusiasm for the method. He brought with him a set of Linton Strippers which are the most widely used instruments in this area today for the surgical eradication of varicose veins.

During the next few years he began to formulate his thinking about the stripping method and realized that not only the main line varicosities were to be taken out but that the dissection of all the intervening branches and incompetent communicating veins must also be eradicated. This course of radical stripping and dissection is still the most universally acceptable method for varicose vein therapy.

The foregoing development took place over a number of years. In 1935 Dr. McPheeters decided to limit his practice to the treatment of peripheral vascular disease, with emphasis on the venous aspect. In this respect, he was probably the first specialist in a field which now has grown to great proportions, that of angiology. As an angiologist, he not only contributed to the surgical therapy of venous disease but also to its medical aspects. It was Dr. McPheeters who developed the idea of the "venous heart"; for example, the pumping action of the muscular movement on the venous blood in the extremity, and he used this principle in the treatment of stasis ulcers by the use of support and exercise. Healing of ulcers on an ambulatory basis was more possible in this way, thereby reducing the morbidity and allowing a patient to be productive while his ulcer was healing.

In most of the hospitals in the city of Minneapolis, the "McPheeters' Hot Pack" still proves to be one of the most important methods in the treatment of acute thrombophlebitis and infected ulcers. Early ambulation, following adequate anticoagulant therapy for thrombophlebitis was another of his contributions. This has reduced the hospital stay and morbidity of this type of patient and has greatly reduced the pain experience following long periods of immobilization and bed rest. It was Dr. McPheeters who developed the idea of walking with adequate support of help to reduce the edema of the postphlebitic leg and to help heal stasis ulcers, once the secondary infection was controlled.

His renown grew and so did his private practice. The demand for him as a speaker began to increase, not only in Minneapolis but throughout the state of Minnesota and into Chicago, New York, and Boston. During his practice he has given approximately 100 talks on the treatment of varicose veins. As a teacher in his chosen field, he became increasingly important. Doctors from the Twin Cities and throughout the state came to visit him, spending weeks in his office, observing his surgical technique. In the years that I was fortunate enough to practice with him I can remember doctors coming from Denver, San Francisco, Chicago, Detroit, Toronto, and Venezuela. Dr. Sieg from Switzerland spent about three weeks with Dr. McPheeters observing his work and discussing the problems of varicose veins. I know that all of these men went away not only impressed with his zeal for the problem but with his desire to give of himself not only to

his patients but also to the doctors who were fortunate to be able to observe him. In addition, they went away with a better knowledge of the problem and the answers to many of their questions.

On Jan. 1, 1917, Dr. McPheeters married Ethel Anderson whom he had met while a student at Hamline University in St. Paul. Their first child was a son, George, and the second was a daughter, Mary. Both children are married; the daughter lives in Minneapolis and the son is personnel manager for the Weyerhauser Co. of Tacoma, Washington. One of Dr. McPheeters' many outside interests is movie photography. The making of movies has been probably his greatest extracurricular activity. He has become especially proficient in the making of travelogs. He always used a tripod and also had a camera standard built into the automobile floor so that he could take pictures directly from the auto. Dr. McPheeters has been, for many years, an active member of the Minneapolis Cine Club. When that club took on the project to put together a movie showing the various aspects of the effects of birth defects and the manner in which these children were taken care of, he volunteered to make the picture. He produced a documentary on Cerebral Palsy for the Cerebral Palsy Society, Inc.

An interest closely connected with this movie-making hobby is the showing of movies to the shut-ins at some of the nursing and old people's homes. He has shown not only his own travelogs but also many others which he thought might be of interest to these people.

It was not an unusual sight to find him selling ice cold pop during the Minneapolis Aquatennial or to discover him ringing the bells at the corner kettles before Christmas. These were some of the projects of the Minneapolis Optimist Club which he joined in 1929 and has been a member of ever since. In 1937 he served on his first committee assignment for that club. That assignment was arranging for the examinations and the medical supplies for the boy campers who were going to the Optimist Kamp Ketchi Kahniss. This project has been his for the past twenty-seven years. From 1942 to 1944, and in 1956, he served on the board of governors of the Optimist Club and was its president in 1956. In this period the club received the Honor Club status from the Optimist International. He was chairman of the new club building committee from 1956 to 1957. During that year, the Southdale Club was formed which became one of the most active suburban clubs.

In 1956 Dr. McPheeters, as president of the Optimist Club, was approached by the Gopher State Timing Association to attempt sponsorship of the building of a drag strip to be located somewhere near the Twin Cities. He became interested in the project and through his great energy and fire he was able to interest the Twin City Optimist Clubs in the project so that a joint sponsorship by eleven of the clubs was accomplished. After much work and "walking all over Anoka County," a site was purchased and work was begun on the strip.

Great obstacles had to be overcome; for example, the land which was suited for the strip was owned by 14 different landowners and each had to be dealt with separately. One man held out, but eventually he yielded and the project was begun in 1957. The strip became operational in 1958 and Dr. McPheeters became its first president. To this date, he is still quite active on the Twin City Drag Strip Board.

Dr. McPheeters' interests were and are varied, and always of great service to the community. One of the greatest acts of benevolence to his fellowmen is his affiliation with the Big Brothers. This organization was set up in 1933 in this area for the purpose of furnishing the fatherless boy with someone to look up to and emulate; a man who would be willing to listen to the boy's problems with understanding and sympathy. That someone would be "a friend of the boy." Dr. McPheeters was appointed to the original board in 1933 and is still on the Big Brothers' Board in Minneapolis. In 1936 he served as vice-president. From 1941 to 1946 he served as a Big Brother, and again from 1953 to 1957. It is interesting to note that from this group of 4 boys, 1 is now a Big Brother himself and has been for the past three years. This man is now a successful attorney. One can only speculate as to what his role in life would be if not for the direct influence of Dr. McPheeters.

Dr. McPheeters is a member of the Hennepin County Medical Society, Fellow of the American College of Surgeons, Fellow of Internal College of Surgeons, Fellow of the American College of Angiology, Fellow of the International College of Angiology, Honorary Member of the American Phlebology Society, and Honorary Member of Venezuela Surgical Society. He is also a member of the Minneapolis Surgical Society of which he was president in 1938. He is a staff member of Asbury Methodist Hospital and Northwestern Hospital in Minneapolis. He was elected president of the Asbury Hospital staff in 1942. He has served on the governing board to Asbury Hospital and on the board of Methodist Hospital for many years.

Dr. McPheeters has spoken before medical societies throughout the country. Many county societies in Minnesota have heard him. He has given generously of his time to carry to them his thorough knowledge of the venous system. He has had the honor of visiting with, and speaking before, medical societies in Venezuela, Mexico, and Hawaii.

Among his contributions to medical literature were 3 movies, 2 on the treatment of varicose veins and 1 on the use of the Padgett Dermatome for skin grafting.

In 1929 he published his first book "Varicose Veins," which was not only an excellent résumé of what was known about varicose veins at that time but also added greatly to the knowledge of venous diseases, especially the venous heart. It had 7 editions. In 1939 he and Dr. James Anderson completely revised his book. The new title was "Injection Treatment of Varicose Veins and Hemorrhoids." The stress on treatment in the monograph was on injection with sclerosing materials and his great contribution was the "empty vein" technique.

In 1947 the varicose vein section of this work was again revised and a detailed discussion of the stripping technique was given. This, with certain modifications, is the technique being used today.

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PHONOCARDIOGRAM enhances differential diagnosis of idiopathic dilation of the pulmonary artery, including such features as normal first heart sound, systolic click, faint or absent pulmonic systolic murmur, wide splitting of the second heart sound, and occasional pulmonary diastolic murmur. Pulmonic stenosis, pulmonary hypertension, patent ductus arteriosus, and ventricular and atrial septal defect can be differentiated in this manner, a study of 8 patients revealed.

JAMES N. KARNEGIS, M.D., and YANG WANG, M.D., University of Minnesota, Minneapolis. The phonocardiogram in idiopathic dilatation of the pulmonary artery. Amer. J. Cardiol. 14:75-78, 1964.

Section on PAIN and DISTRESS

Editor: JOHN S. LUNDY, M.D., Seattle, Wash.; *Co-Editor:* RALPH M. TOVELL, M.D., West Hartford, Conn.; *Associate Editors:* ROBERT R. JONES, M.D., Rochester, Minn., JOSEPH A. GIBILISCO, D.D.S., Rochester, Minn., FLORENCE A. MC QUILLEN, C.R.N.A., Chicago, Ill., LLOYD MOUSEL, M.D., Seattle, Wash.

A contribution to understanding

THE SPECIAL ARTICLE in this issue entitled "The Differential Diagnosis of Atypical Facial Pain" by Drs. Gibilisco, Goldstein, and Rushton is on a provocative subject. The problem is presented in considerable detail and makes one conscious of the difficulties that the clinician faces when he suddenly realizes that the patient may have more than one of the conditions listed in the article.

The problem of psychogenic atypical facial pain is one that haunts the investigator from beginning to end in the care of these patients. This becomes an acute problem when the patient has gone from diagnostician to diagnostician in the hope that he may be relieved, and has tried almost everything that is currently available. The patient discusses his problems in such a state of hopelessness that even an optimistic physician becomes somewhat discouraged.

When this point is reached and one is concerned as to whether he has omitted something from consideration, an article such as this is of considerable value.

In the book review portion of this issue, a unique book is reviewed: "Milestones of Anesthesia, or, Readings in the Development of Surgical Anesthesia 1665 to 1940" by Frank Cole, M.D. The author has elected to consider 45 subjects and the persons prominently identified with each problem. This book is well worth reading by anyone with a historical bent. It covers some of the most important phases of anesthesiology, even though that word is not used since it is of such recent origin. There are few people who cannot in some way be concerned with anesthesia or blood transfusion. The beginnings of the solutions of these and associated problems are presented in a fascinating manner. It required much time and effort on the part of the author to isolate the portions that he has selected to print in this anthology. Many readers will wish to go back to the original publications for an elaboration of how these pioneers attempted to solve problems in fields that were then absolutely new.

Observations on the development of the field of anesthesia over the last forty years is of real interest to medical historians, and to us all. Dr. Hans Killian, a man with an established surgical reputation who has kept a lively interest in anesthesia, has written a book that expresses his views on this subject. He has traveled abroad and in his own country, Germany, and has presented a fine work on his subject. He has included a number of photographs of individuals who he feels have contributed significantly to the progress of anesthesia over the years.

JOHN S. LUNDY, M.D.

The Differential Diagnosis of Atypical Facial Pain

JOSEPH A. GIBILISCO, D.D.S., NORMAN P. GOLDSTEIN, M.D., and JOSEPH G. RUSHTON, M.D.

Rochester, Minnesota

MANY PAINFUL CONDITIONS involving the structures of the head present complex diagnostic challenges. The term "atypical facial pain" has been applied to this ill-defined group of conditions, but this term does not refer to trigeminal neuralgia, glossopharyngeal neuralgia, postherpetic neuralgia, or pains caused by obvious diseases of the teeth, throat, nose, sinuses, eyes, and ears. Thus, this leaves a group of conditions characterized by pain that is deep, poorly localized, and vaguely described by the patient. The pain may be felt in regions supplied by the fifth and ninth cranial nerves and second and third cervical nerves. The distribution of the pain is often unanatomic in that it may involve portions of the sensory supply of two or more of these nerves and may cross the midline.

In general, this pain is constant and persists for long periods—that is, weeks to years. Trigger zones are lacking. Patients often describe the pain as "boring," "drawing," "pressing," "pulling," "burning," or "aching." The term "atypical facial pain" is much like the terms "fever" and "convulsion." It names a symptom but does not imply a definite origin or cause. In order to better understand the etiology and treatment of such conditions, we previously studied and reported the clinical data from 100 patients who had the initial diagnosis of atypical facial pain.[1] We have enlarged the study and now present our findings from a group of 190 patients. The condition in each of these 190 patients is classified under one of three headings: psychogenic, organic, or indeterminate. This classification was not made on the basis of any preconceived notions concerning etiologic factors or pathologic conditions. The rationale for such a classification may become clear as we describe each of these headings and discuss them (Table 1).

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PSYCHOGENIC ATYPICAL FACIAL PAIN

The 53 patients (46 women and 7 men) with psychogenic facial pain suffered from depressive reactions, conversion hysteria, or schizophrenia. Each of them complained primarily of facial pain. Other symptoms indicative of psychiatric illness were elicited after some time had been spent in consultation with these patients. The age at onset of the pain varied from 12 to 70 years, the majority of patients being in the fourth and fifth decades of life. The duration of pain varied from one to thirty-six years. Only 8 patients reported any remission of pain; 3 of these could give no reason for remission, 1 had pain only during her menstrual flow, and the remaining 4 had noted temporary relief after minor surgical procedures on the nose, sinuses, or teeth. The other patients in the group had constant pain. None was addicted to the use of opiates. Sixteen of these patients could obtain partial relief from the use of mild analgesic or sedative agents but, in each instance, the relief was so unsatisfactory that none had become habituated to the drug giving this partial relief.

A total of 33 patients were unable to recognize any cause for their pain. The presumed causes offered by the remaining 20 patients were as follows: dental operations, 11; being struck in the face by husband, 3; husband's illness, "nervous breakdown," nasal operation, parotitis, infected ear, and operation on the trigeminal nerve, 1 patient each.

We are reluctant to use the term "psycho-

genic." However, the unusual character and unanatomic distribution of the pain, the lack of any signs of organic derangement, and the prominence of symptoms indicating emotional illness justify the label.

ORGANIC ATYPICAL FACIAL PAIN

In this group of patients the pain apparently resulted from an actual morbid anatomic change, such as neoplasm, or from obviously disturbed physiological function, such as vasodilatation. These patients could be subdivided into 6 subgroups according to whether they had: (1) vasodilating facial pain, (2) dental diseases, (3) neuropathy, (4) neoplasm, (5) subacute thyroiditis, or (6) miscellaneous conditions.

Vasodilating facial pain. Seven men and 1 woman had pain thought to be the result of dilatation of arteries of the face. This pain closely resembled histaminic cephalalgia or "cluster" headache in character, onset, and duration, but the location was sufficiently unusual to cause some difficulty in recognition. The maximal pain was in the lower portion of the face, which contrasts to the location in the usual case of histaminic cephalalgia. The attacks were relatively brief (twenty minutes to three hours) and usually occurred several times in twenty-four hours. Repeated bouts of pain would trouble the patient for days or weeks at a time and then subside to leave him free of pain for several weeks or a year. In each case, a trial injection of ergotamine tartrate relieved the pain of an attack. Six of these patients had had a previous diagnosis of trigeminal neuralgia. Various surgical procedures had been performed on six patients to relieve the pain. These operations included extraction of teeth, operations on the nose and paranasal sinuses, injections of alcohol, and avulsion of branches of the trigeminal nerve. One patient had the dubious distinction of having undergone 10 separate operations on his face; each was done for the purpose of relieving pain, and each was a total failure.

TABLE 1
CLASSIFICATION OF ATYPICAL FACIAL PAIN IN 190 PATIENTS

	Male	*Female*	*Total*
Psychogenic	7	46	53
Organic	47	76	
Vascular	7	1	
Dental	1	7	
Neuritic	29	32	
Neoplastic	1	2	
Subacute thyroiditis	9	31	
Miscellaneous	0	3	123
Indeterminate	5	9	14
Total			190

Dental disease. Atypical facial pain was proved to be caused by previously unrecognized dental disease in 8 patients. In each instance the pain was unusual, and objective evidence for dental disease was lacking during the early part of the illness. The pain was described as a constant ache in the face, but not in the teeth, by 4 patients and as a severe but intermittent ache by 4 patients. Two patients noted that hot or cold foods or liquids would increase the pain. Spontaneous remissions of pain were noted by 6 of the patients. Seven patients experienced some relief with the use of ordinary analgesic agents. In general, the pain was poorly localized; in no case was it localized to the offending tooth until late in the course of the illness. Physical examination and roentgenologic studies early in the illness gave normal results. Subsequent dental examinations disclosed the dental disease. In 5 patients the final diagnosis was pulpitis, and the pain was relieved by extraction of the tooth. Three patients had causalgia of the mandibular nerve. Their discomfort was not relieved by treatment.

Neuropathy. We have defined trigeminal neuropathy as a condition in which there is more or less prolonged disorder of sensation (and occasionally of motility) which is confined to the distribution of the fifth cranial nerve, either unilaterally or bilaterally. Trigeminal neuritis is a form of neuropathy in which the lesion presumably is caused by an inflammatory reaction. Since it is extremely rare to have histologic proof of an inflammatory reaction in this nerve, it seems advisable to accept clinical or laboratory evidence of an inflammation of the nerve as justification for the term "neuritis." Trigeminal neuralgia is characterized by brief attacks of sharp, lancinating pain in the distribution of the trigeminal nerve. In contrast, the pain of trigeminal neuropathy is described as an ache or burning, boring, pulling, drawing sensation, and, at times, a feeling of pressure. Pain may be present constantly. Differentiation between trigeminal neuropathy and trigeminal neuralgia is important because of the difference in appropriate therapeutic measures. Whereas the usual therapy of trigeminal neuralgia consists of either injection of alcohol into the nerve or a surgical procedure, therapy for trigeminal neuropathy is as varied as are the causes of the disorder. Some of these causes are benign in themselves, while others are extremely serious; hence, an intelligent approach to therapy of trigeminal neuropathy is dependent

TABLE 2

TRIGEMINAL NEUROPATHY: CAUSES AND CLINICAL DATA IN 61 CASES*

Causes	Cases, No.	Sex		Age range, year	Duration of symptoms before examination
		Male	Female		
Dental surgery	21	11	10	28-68	1 week to 16 years
Denture pressure	8	1	7	49-76	2 months to 10 years
Surgical (not dental) or mechanical trauma	8	5	3	14-68	1 month to 27 years
Stilbamidine	7	3	4	30-63	1 month to 7 years
Miscellaneous	10	7	3	27-72	1 week to 5 years
Unknown	7	2	5	19-66	1 month to 21 years

*Reproduced with permission from GOLDSTEIN, N. P., GIBILISCO, J. A., and RUSHTON, J. G.: Trigeminal neuropathy and neuritis: A study of etiology with emphasis on dental causes. J. Amer. med. Ass. 184:458-462, 1963.[2]

on going beyond the diagnosis to an understanding of the cause in each case.

With this in mind, we studied 61 cases in which the history and clinical findings led to a diagnosis of trigeminal neuropathy.[2] We separated these cases into 6 categories based on the presumed causes as shown in table 2. Twenty-one patients had experienced onset of symptoms after a dental procedure; the neuropathy was associated with tooth removal in 17, and in 4 it was due to injury to sensory fibers of the trigeminal nerve as a result of needle puncture. The usual complaint was paresthesia, but several of these patients had pain as well. In 9 patients in this group, difficulty developed after removal of impacted mandibular third molars. The incidence is explained by the close proximity of the roots of this tooth to the inferior alveolar nerve. In some instances the sensory fibers may course between the roots of the teeth, making trauma to this nerve unavoidable and neuropathy a frequent sequela of extraction. In 8 patients, neuropathy developed after extraction of teeth other than mandibular third molars. Usually, the neuropathy was preceded by a postoperative complication such as alveolar osteitis or over-zealous and repeated treatment of the wound when the patient was concerned about slow healing or persistent discomfort. The 4 patients whose neuropathy resulted from needle trauma to the sensory fibers during injection of a local anesthetic described paresthesias within the mandibular division. One of them also complained of pain.

Another cause of neuropathy was denture trauma. Alveolar resorption commonly occurs after the loss of teeth. Should the resorption continue until the mental foramen is approximated, pressure trauma to the mental nerve may occur. In this series of 61 patients with trigeminal neuropathy, denture trauma was the cause of symptoms in 8 patients; 4 of them experienced pain alone, 1 reported paresthesia alone, and 3 complained of both pain and paresthesia. Only the third division was affected in any of these patients.

Trigeminal neuropathy may occur after surgical procedures on the face or mechanical trauma to the face. Among those whose neuropathy resulted from extraoral surgical procedures, 1 patient noted onset after dissection of the right submaxillary gland, 1 after an operation in the right antrum for sinusitis, and 1 after biopsy of the right mandible because of swelling and pain in the jaw. In still another patient the neuropathy was noted after injection of alcohol into the first and second divisions of the right trigeminal nerve to terminate an ill-defined facial pain. Of those patients who had suffered some type of mechanical trauma to the face and subsequent neuropathy, 1 had received numerous lacerations and abrasions of the face in an automobile accident, 1 had been kicked in the face during a football game, 1 woman had been hit in the right eye and forehead (with supraorbital neuropathy resulting), and 1 had received a blow to the mouth.

An outstanding side effect or complication followed the use of stilbamidine isothionate, a drug no longer in wide use. Trial of this drug as a method of treatment for trigeminal neuralgia was based on its capacity to cause sensory neuritis. Seven of our 61 patients with neuropathy had paresthesias of the face, which developed subsequent to the use of stilbamidine. The drug had been given for trigeminal neuralgia in 3 patients, for blastomycosis in 2, for pain in the ear after herpes zoster in 1, and for multiple myeloma in 1. All patients in this group had paresthesias of both sides of the face, which involved all the divisions of the trigeminal nerve, and 3 patients had pain as well as paresthesias. In addition, 2 patients noted involvement of the upper part of the neck; 1 was troubled with paresthesias of the neck, arms, and upper half of the torso anteriorly and posteriorly. The development of the paresthesias from the degree first noted to maximal intensity took from one week to two months.

Ten other instances of trigeminal neuropathy arose from a variety of causes, no single cause producing enough cases to justify separate consideration of the data. Three of the patients had tumors that involved the head or neck. There were 2 instances in which the trigeminal neuropathy resulted from intracranial aneurysms. In 2 instances the neuritis seemed to have been caused by a viral infection. One patient had had a sore point on his tongue, and the symptoms of trigeminal neuropathy started in the tongue approximately one week after his physician had applied silver nitrate to this location. In another man, left trigeminal neuropathy developed after he was stung on the left lower eyelid by an insect. Still another man had trigeminal neuropathy that involved all three divisions bilaterally. This seemed to be related to tabes dorsalis as a part of a more generalized illness. A group of 5 women and 2 men had trigeminal neuropathy of unknown cause.

When a patient has trigeminal neuropathy, there is likely to be some history of trauma to the trigeminal nerve. The importance of the dental structures and dental procedures as the cause of trigeminal neuropathy is apparent, since, in almost half of our patients (48%), trigeminal neuropathy developed as a consequence of some dental problem. It is also apparent that thorough physical examination is indicated in cases of trigeminal neuropathy.

Neoplasms. One of the major benefits to be derived from a classification of types of atypical facial pain such as has been attempted here is the possibility that it will eliminate the use of the term "atypical facial pain" as a synonym for "functional" or "psychogenic pain." Although slightly more than one-fourth of the patients with atypical facial pain do have pain that may be called "psychogenic," there were a few that proved to have neoplasms. We found 3 patients with neoplasms that caused unusual pain. Two women had suffered from facial pain for five and six years, respectively, before other evidence of a tumor became apparent. Each had a cylindroma, 1 in the parotid and 1 in the antrum. In each patient, careful and repeated examinations had failed to disclose any abnormality until late in the course of the illness. In each of these 2 patients the pain was deep, shooting, and boring but poorly localized. It was present constantly but varied unpredictably in severity. The third patient with a tumor, a man, had noted a variety of aching, jabbing, and burning pains on one side of his face for one year during which time no cause for his distress could be discovered. His pain did not resemble trigeminal neuralgia. After a year he became aware of numbness on the painful side of his face. Diminished sensation was found on testing with a pin and cotton. A neurofibroma of the acoustic nerve was recognized and removed.

TABLE 3
SYMPTOMS OF SUBACUTE THYROIDITIS IN 40 CASES*

Symptoms	*Cases*	*Percent of total*
Tender neck	24	60
Preauricular pain	16	40
Pain in jaw	15	37
Malaise and loss of weight	14	35
Pain on swallowing	13	32
Headache	8	20
Pain in arm and shoulder	4	10
Pain in teeth	3	7
Face pain	2	5

*Reproduced with permission from TOLMAN, D. E., GIBILISCO, J. A., and MC CONAHEY, W. M.: Subacute thyroiditis: A diagnostic possibility for the dentist. Oral Surg. 15:293-295, 1962.[3]

Subacute thyroiditis. The frequent appearance of pain in the head and neck in persons with subacute thyroiditis justifies its classification as atypical facial pain. An analysis was made of 40 cases in which a diagnosis of subacute thyroiditis had been made at the Mayo Clinic in 1955 and 1956.[3] A high percentage of these patients complained of preauricular pain and pain of the angle of the mandible (Table 3).

Early recognition of subacute thyroiditis is of primary importance, but the early diagnosis is difficult. Not infrequently the patient is treated for pharyngitis or a similar condition while the thyroiditis runs it course.

The dental profession can play an important part in the early recognition of this disorder because pain in the jaw is a symptom in a significant number of patients. Perhaps of even greater importance is the fact that 2 patients in this series sought dental treatment and 1 had several teeth extracted before the establishment of the correct diagnosis. In all patients of this series, jaw pain subsided with treatment of the subacute thyroiditis.

Miscellaneous. Three patients with atypical facial pain had organically caused pain as a result of a variety of conditions. In each instance the pain was unusual and other manifestations of the presumed cause were not readily apparent. A young woman with acromegaly had pain on the right side of her face for sixteen months. Her discomfort resembled trigeminal neuralgia in some ways but was not typical of that condition. The sensation on the affected side of the face was diminished. Section of the sen-

sory root of the trigeminal nerve relieved the severe stabbing pain but left a constant burning discomfort on the right side of the face. The second patient was a woman who had sudden severe pain in the right eye with diminution but not complete loss of vision in that eye. When examined three weeks later, she was found to have temporal arteritis. The third patient, a woman, had a stroke with hemiplegia on the right and pain over the entire right side of the body. Within a few months the pain disappeared except for soreness and burning of the gums, tongue, and malar region on the right side. At the time she was last seen at this clinic, the condition had persisted for two years. The pain was assumed to have been a result of a thalamic lesion.

INDETERMINATE ATYPICAL FACIAL PAIN

Of the group of 190 patients that were studied, 13 were classified as having pain of indeterminate cause. They were so classified largely because they failed to qualify for either the psychogenic or the organic group. In more than half of these patients, the onset of pain was after the age of 50 years. The duration of pain was relatively short as compared with that in the psychogenic pain group. Presumed causes for the pain include infections, injuries, and operations about the face. Some patients did not recognize any cause for the pain. In general, the pain experienced by these patients had the following characteristics: short duration and onset late in life compared to the other two groups. Remissions were common and the pain was made worse by maneuvers such as chewing, rubbing the face, or moving the head. The increased discomfort induced by these maneuvers is generally associated with pain of organic origin. Most of the patients could gain temporary but substantial relief by taking ordinary analgesic agents. There was no reliable evidence to indicate that the pain was psychogenic, and the character of the pain did suggest an organic cause.

DISCUSSION

Our experience suggests various conditions that may be associated with atypical facial pain but offers no easy solutions to the problems of diagnosis and treatment. The physician's chief concern should be to establish a diagnosis. This begins with a detailed history of the complaint. This seems trite but is of great importance. In most cases, few abnormalities will be discovered in the physical examinations or laboratory tests. When such abnormalities are found, caution must be used in considering them to be the cause of the pain. For example, chronic paranasal sinusitis may be present but have no relationship to the pain. The discovery, on physical or laboratory examination, of an abnormality which probably accounts for the pain may open the way to successful treatment.

If a diagnosis cannot be made with reasonable certainty, treatment should be conservative. The rash use of surgical measures often worsens the situation by compounding the types of pain. The attitude of the physician will have much to do with the future well-being of the patient. A brusque announcement that "Nothing is wrong" may solve the physician's problem because the patient will leave the office firmly resolved not to return. The same information can be conveyed in a manner which reassures the patient that careful examination has not revealed any evidence of serious disease. This should be followed by the physician's assurance that he recognizes the difficulty experienced by the patient and will continue to do all that is practical to be of aid. The use of nonnarcotic analgesic agents, tranquilizers, and appropriate physical therapy should be accompanied by an explanation that the measures are not curative. This approach will avoid undue optimism and will allow for changing the regimen from time to time. Such an approach assures the patient of the continued interest and support of the physician who, in turn, is allowed the privilege of periodic reexamination of the patient with the result that a previously undetected lesion may be recognized early and treated properly.

Inasmuch as the causes of the various syndromes of atypical facial pain are so variable, ranging from psychiatric disorders to various diseases of the structures of the head and face, these conditions cut across the boundaries of different specialties of medicine and dentistry. At times, multiple consultations among internists, otorhinolaryngologists, ophthalmologists, neurologists, psychiatrists, and dentists are required; at other times, the cause of the atypical facial pain is quite apparent and special studies are not needed.

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Pain of Dental Origin

RAUL VILLARREAL DE LA GARZA, D.D.S., and
MARIA ANGELICA TAMEZ DE VILLARREAL, D.D.S.
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FACIAL PAIN of obscure etiology is sometimes originated from dental pathology. For this reason a dental consultation should be recommended in these cases. In dental practice the pulpometer is a valuable examining aid. It is an instrument used to test the sensitivity of the pulpal organ. It is the opinion of the authors that results are more accurate than those elicited by the thermal test. The instrument consists essentially of 2 electrodes. One is held by the patient while the other is applied over the surface of the tooth being tested. The voltage of the electrical current is graduated and the threshold of sensitivity is determined. Abnormal findings in response to this stimulus are ascribed to pathological changes of the dental pulp. These changes are, in turn, evaluated so that the proper treatment may be formulated.

A series of 5 patients with facial pain of obscure origin is presented. The pulpometer test was particularly useful in making the correct etiological diagnoses. A treatment which proved successful in each case was carried out.

Case 1. A 22-year-old man was seen on June 4, 1960, complaining of sharp pain along the left mandible of one-half-hour duration. Clinical examination of the teeth was essentially negative. Pulpometer test focused our attention on the second left inferior molar tooth because of its increased threshold of sensitivity. A very small piece of tinfoil, such as the kind used to wrap candy, was then found impacted on a silver alloy filling of the tooth. Removal of the tinfoil was followed by dramatic relief of pain. Irritation of the dental pulp by electrolysis between 2 bodies of different metals caused the symptom.

Case 2. A 19-year-old stenographer was examined on June 15, 1964, complaining of pain in the right frontal region and right cheek during a period of nine days. The pain was constant in the daytime, starting one or two hours after awakening. It was of moderate severity and had acute exacerbations related to meals. Clinical examination revealed a faulty occlusion of a filling of the first right inferior molar tooth where the pulpometer test showed increased sensitivity. Correction was obtained by grinding the highest point of the filling. The pain subsided following this.

Case 3. A 46-year-old housewife was examined on April 17, 1962, with an eight-month history of severe pain in the left frontal region, left periorbitary region, and, left cheek. The episodes were of several hours' duration and were precipitated at times by the ingestion of cold drinks. The patient had been under the medical care of 2 physicians; their prescriptions consisted chiefly of vitamin B_1 and vitamin B_{12} and sedatives. Clinical and laboratory studies had yielded essentially negative findings. Our examination revealed periodontosis with moderate resorption of the alveolar bone. The pulpometer test disclosed findings consistent with severe pulpitis of the first and second left superior molar teeth. The crises of pain subsided following the removal of these teeth. This patient was last seen on June 10, 1964, and still was asymptomatic.

Case 4. A 30-year-old housewife came to our office for the first time on May 16, 1962, complaining of the dislodgement of a filling which had been applied one month earlier. Further questioning disclosed a chronic history of episodes of facial pain during a period of twelve years. Each episode was approximately of one week's duration and occurred at intervals from one to three months. The pain was excruciating, constant during each episode, and had exacerbations precipitated by moving the lips, by low-

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ering the head, or by gently touching the cheeks. The pain was localized in the forehead, both periorbitary regions, both cheeks, superior jaw, and upper lip. It was associated with a feeling of numbness in the lower lip and mandible. The patient had received treatment on different occasions from 5 physicians. The medication had consisted chiefly of sedatives and vitamin B_1.

Our examination revealed a faulty occlusion of the first and second left superior molar teeth and also of the first and second right superior molar teeth. The findings with the pulpometer were consistent with severe pulpitis in these 4 teeth. A balanced occlusion was carried out. One week later the patient developed facial pain but on this occasion the symptoms were definitely decreased in severity. Encouraged by this, and in view of the fact that the pulpometer test still showed pulpitis, the first and second right superior molar teeth were removed. Disappearance of the symptoms on the right side followed. Two days later the first and second left superior molar teeth were also removed. The remaining symptoms subsided. This patient has not shown any recurrence of pain since that time. She was last seen on June 28, 1964, and was still asymptomatic.

Case 5. A 32-year-old man was seen on March 24, 1963, with the history of facial pain crisis occurring at intervals from two to ten days during the past four years. The pain was severe and localized in the right cheek. Each crisis was of several hours' duration. The patient, a physician himself, had received treatment from 3 other physicians with only temporary improvement. He had undergone an extensive clinical and laboratory work-up which proved negative. We were able, by the aid of the pulpometer, to disclose a pulpitis in the second right superior molar tooth which originated from a faulty occlusion. This was corrected by a balanced occlusion. The pain subsided and had not recurred at the last follow-up examination on June 30, 1964.

SUMMARY

Dental pathology is sometimes the cause of facial pain of obscure origin. A series of 5 cases is presented in which the symptoms subsided following the correction of the dental condition. The pulpometer, used in dental practice to test the sensitivity of the pulpal organ, was a valuable aid in making the correct diagnoses.

Book Reviews on Pain . . .

A SYNOPSIS OF ANESTHESIA, *Fifth Edition by* J. ALFRED LEE *and* R. S. ATKINSON, *774 pp., ill., Williams & Wilkins Co., Baltimore, Md. $9.50*

This book, prepared with English exactness of over 700 pages and 34 chapters, briefly presents encyclopedic information on most of the subjects that might be looked up by anyone in anesthesia, beginner or experienced person. The first chapter is entitled "Notes on the History of Anaesthesia" and presents some unique information.

Other chapters are "Some Anatomical and Physiological Notes;" "Preanaesthetic Care and Preparation;" "The Pharmacology of Drugs Used for Preoperative and Post-Operative Medication;" "Inhalation Anaesthesia;" "The Anaesthetic Gases" "Volatile Anaesthetic Agents;" "Artificial Ventilation of the Lungs;" "Accidents of Inhalation Anaesthesia and How to Treat Them;" "Gases Used in Association with Anaesthesia;" "Endotracheal Anaesthesia;" "Intravenous Anaesthesia;" "Analeptics, Antagonists, and Pressor Agents;" "The Phenothiazine Derivatives;" "Spinal Analgesia;" "Regional Anaesthesia;" "The Use of Muscle Relaxants in Anaesthesia;" "Hypnosis and Electrical Anaesthesia;" "Choice of Anaesthetic, as Influenced by Type of Operation;" "Anaesthesia for Neurosurgery;" "Anaesthesia in Thoracic Surgery;" "Paediatric Anaesthesia;" "Choice of Anaesthetic Agents and Methods as Influenced by General Condition of Patient;" "Shock;" "The Complications and Sequelae of Anaesthesia;" "Production of Ischaemia During Operations;" "Explosion Risks in Anaesthesia;" "Induced Hypothermia;" "Care of the Anaesthetized Patient;" "Monitoring During Anaesthesia;" "Anaesthesia and Analgesia in Labour;" "Therapeutic Aspects of Anaesthesia;" "Post-Operative Observation Room;" "Care and Sterilization of Equipment."

After Chapter 34 comes an appendix and index.

This book is printed in relatively fine print. The pages are small. There are a number of illustrations of apparatus, and a number of tables that are concerned with subjects such as "Properties of Some Inhalation Anaesthetics."

Although sometimes the explanation to the reader's question may be brief, references are made so that he can obtain more detailed answers to his question if he wishes to.

This book has the most ambitious coverage of the subject of anesthesia that has yet appeared.

J. S. LUNDY, M.D.
Seattle

FORTY YEARS OF ANESTHESIA EXPERIENCE *by* DR. HANS KILLIAN, *294 pp., Verlag Der Deutschen-Hochschullehrer-Zeitung-Turingen, 1964.*

This is one of several books that the author has published in the last few years and is of special interest to those of us in anesthesia specialty in the United States, since Dr. Killian is an accomplished surgeon and has had a

great interest in anesthesia throughout his life. In his travels he has been able to observe anesthesia in this country and in European countries, and his story of this experience is very interesting. It is to be hoped that the book will be published in English. It consists of twenty-nine chapters.

In addition, there is a special bibliography and an author index. It has been illustrated by colored plates showing the bizarre effects of anesthetics on people. A number of pictures are shown of those individuals who have particularly caught the attention of the author.

The book is well printed on good paper, is easily read, and should be brought to the attention of those individuals who are interested in the German point of view on the question of anesthesia.

JOHN S. LUNDY, M.D.
Seattle

THE HISTORY OF SURGICAL ANESTHESIA, *by* THOMAS E. KEYS, *193 pp., ill., Dover Publications, Inc., New York City, 1963. $2*

It is a happy circumstance that at last one may obtain, for as little as $2, the story of what must surely be the most important American contribution to the practice of medicine and surgery, meaning anesthesia. The chronicle has ben revised and expanded in detail since the basis of it was first printed in my volume, *Clinical Anesthesia,* in 1942. The formal book version appeared in 1945, and certain aspects of that work will be revised again for inclusion in a book, *Local, Regional and Spinal Anesthesia,* to be issued in 1965, and to be edited by me.

Any reader—even one who knows nothing about medicine—could scarcely fail to find some interest in this small book, because almost no one is free of the possibility that some day he may have to be anesthetized or, if he is not, some member of his family or one of his friends may have this experience. This book deserves inclusion on any shelf devoted to books on history, and it would be an unusual and an instructive gift to a person of whatever taste in reading. It would be, moreover, very useful to someone who is preparing for an examination in a medical subject. This is a book which should be a part of the personal library of physicians in almost any specialty of medicine or surgery.

JOHN S. LUNDY, M.D.
Seattle

MILESTONES IN ANESTHESIA: *Readings in the Development of Surgical Anesthesia 1665-1940 by* FRANK COLE, M.D., *290 pp., University of Nebraska Press, Lincoln, Neb., 1965. $6.50*

This volume is a timely contribution to anesthesiology. The author has carefully read a thousand articles in making selections for inclusion in the book. The meticulous care involved in its preparation represents a part of the tradition of the workers in this special field that has, in the relatively short space of a hundred years, become established as a specialty of medicine and surgery.

It has been difficult for most medical men to acquire cultural as well as scientific knowledge; and since scientific knowledge has been the first prerequisite, the cultural aspects have been allowed to wait. This volume makes it not only possible but convenient to acquire some of those cultural aspects that are as important to the seasoned practitioner as to the beginner in anesthesiology. The scientific importance of the book can hardly be estimated yet, but the volume should enable all of us who are interested in research and clinical anesthesia to acquaint ourselves with the name of each innovator and with his contribution—how he made it, when he made it, where he made it, and why he made it.

This book should be a valuable source of information for all of us, but it should be particularly so for those who are entering the field, that they may from the beginning understand the scientific background and the other factors which have influenced the relatively rapid development of anesthesiology. By presenting to us its history in the words of those who made it, Dr. Frank Cole has made a contribution which of itself will come to be recognized as outstanding in the progress that has been and will be made in the field of anesthesiology.

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This book is not indexed and there are no illustrations. It is well printed on good paper and is easily read.

JOHN S. LUNDY, M.D.

POST-LUMBAR PUNCTURE HEADACHES, *by* WALLACE W. TOURTELLOTTE, ARMIN F. HAERER, GRANT L. HELLER, *and* JOHN E. SOMERS, *120 pp., ill., Charles C Thomas, Springfield, Ill., 1964. $5.50*

This small book, with a foreword by Dr. DeJong, is a timely discussion of a controversial subject that has long been ready for some kind of at least a semifinal decision. The findings and the questions and answers included in the text are based essentially on neurological interests. The points made are not directly formed by those interested in anesthesia; at least no representative of that department is listed among the authors. The reason is not given.

However, the book is well printed on good paper, is indexed, and is easily read. The areas covered are (1) historical information, (2) incidence and modifying factors of the postlumbar puncture headaches in 135 normal individuals, with case reports, (3) incidence and modifying factors of postlumbar headaches in 317 neurological patients, in 100 patients undergoing spinal anesthesia and in 13 patients undergoing epidural anesthesia, (4) incidence of postlumbar headaches and effect on the course of 80 patients with multiple sclerosis, and (5) summary discussion.

It is hard to find fault with this book. The treatment for postlumbar puncture headaches is correct and practical and "it works." A few semiserious statements are included, such as Lundy blames the headache on eyeglasses, which of course I did not. I suggested long ago when we knew little about this subject that we should check everything we could think of, even eyeglasses, though that was unlikely.

JOHN S. LUNDY, M.D.
Seattle

HANDBOOK OF THE PRACTICE OF ANESTHESIA, *by* JOHN R. S. SHIELDS, *203 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1963. $6.85*

This small book bases its content on the fact that there are no major or minor anesthesia methods; all carry the weight of life or death for the patient. The author makes the most points with the fewest words on the subjects of

1. *Preoperative considerations.* Evaluation and premedication of the patients and preparation for the anesthetic

2. *General anesthesia.* Administration, muscle relaxant drugs, problems arising during anesthesia, and monitoring during anesthesia

3. *Special techniques.* Conduction anesthesia and pediatric anesthesia. Induced hypotension and hypothermia

4. *Unusual problems* associated with the surgery or the patient's condition. Conditions that present special problems in anesthesia. Resuscitation following respiratory or cardiovascular failure

5. *Postoperative care and fluid therapy.* The book is indexed and is printed on good paper. There are over 100 fine illustrations which alone make this book especially valuable to both teacher, student, and practitioner.

JOHN S. LUNDY, M.D.
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Current Literature on Pain . . .

BELLVILLE, J. W. and GREEN, JEAN: *The respiratory and subjective effects of pentazocine.* Clin. Pharmacol. & Therap. 6:152-159 (March-April) 1965.

"Pentazocine . . . (Win 20,228), has been found to be a potent analgesic in man and to have low addiction liability. . . . This study was done to define precisely the relative potency in terms of respiratory effects and to determine whether pentazocine has any relative advantage over morphine as far as these properties are concerned. Subjective effects were also recorded before and after drug administration to discern if there were qualitative differences between morphine and pentazocine. . . . Six male volunteers free of respiratory and cardiovascular disease served as subjects for this study. . . .

"The relative respiratory depressant potency of pentazocine . . . was found to be 0.47 with upper and lower 95 percent confidence limits of 1.10 and 0.26. Pentazocine appeared to have a time-effect curve differing in appearance from that of morphine. It achieved a higher peak and more rapid falloff than an equivalent dose of morphine. Subjective effects similar to those produced by morphine were noted although there appeared to be qualitative differences in that the subjects seemed more anxious following pentazocine."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

BRIDENBAUGH, L. D., MOORE, D. C., and CAMPBELL, D. D.: *Management of upper abdominal cancer pain. Treatment with celiac plexus block with alcohol.* J.A.M.A. 190:877-880 (Dec. 7) 1964.

"The management or control of intractable pain in patients who have a nonresectable or recurrent carcinoma of the stomach, pancreas, liver, or gallbladder is often a major problem for the surgeon or responsible physician. . . . Since 1948, at our institution [Mason Clinic, Seattle] this type of pain has been managed by means of celiac plexus block with alcohol. A study was made of patients who had received this treatment to evaluate the effectiveness of, and the problems resulting from, the procedure. . . .

"The records disclosed that 41 patients had intractable pain from cancer of the stomach, pancreas, gallbladder, or liver, which was found to be nonresectable at the time of surgery. . . . All were given a bilateral celiac plexus block in which 40 to 50 cc. of 50% alcohol was used. With the exception of one patient, all were free from pain for a time varying from six weeks to one year. . . . The disease seldom exceeded this duration. If the pain did recur, extensive metastases had usually occurred outside the area of the block. The single patient who apparently was not benefited by the block was believed to have been addicted to narcotics before the block was done."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

CORSSEN, GUENTHER, DOMINO, E. F., and SWEET, R. B.: *Neuroleptanalgesia and anesthesia.* Anesth. & Analg. 43:748-762 (Nov.-Dec.) 1964.

"For more than a century it has commonly been accepted that general anesthesia can safely protect an organism from surgical pain only if cortical and subcortical centers are effectively depressed. The efficacy of agents used to produce such an anesthetic state has been judged according to how fast they could induce optimal cerebral depression with minimal circulatory, respiratory, and metabolic derangements, and how readily their effects could be overcome.

"Laborit first drew attention to the need for revising the old conventional approach to general anesthesia when he introduced a new concept based on selective blocking of certain cellular, autonomic, and endocrine mechanisms normally activated as a response to stress. . . .

"The study . . . which was carried out at the University of Michigan Medical Center, was undertaken to clarify the human pharmacologic actions of dehydrobenzperidol and phentanyl and to investigate the clinical usefulness of these agents in various types of surgical operations. . . .

"In appropriate dosages given intravenously, the butyrophenone derivative dehydrobenzperidol and the narcotic analgesic phentanyl produced a state of semiconsciousness or 'mineralization' in which patients lay resting and unresistant during surgery. With the addition of nitrous oxide-oxygen mixtures to cause sleep and memory deficit, and muscle relaxants to reduce muscle tone, it was found that any type of minor or major operation could be performed. During prolonged operations, small additional amounts of phentanyl were sufficient to ensure adequate analgesia.

"As used in 359 cases, this technic ('neuroleptanalgesia') was particularly valuable in the treatment of elderly and poor-risk patients. Also it offered distinct advantages over conventional anesthetic methods for patients undergoing repair of intracardiac defects with the aid of extracorporeal circulation.

"Cardiovascular stability was remarkable throughout prolonged and especially traumatic procedures. The alpha-adrenergic blocking action of dehydrobenzperidol appears to be advantageous in cases complicated by massive blood loss or by shock.

"Postanesthetic recovery was fast and smooth. Freedom from pain extended well into the postoperative period; if narcotic analgesics were eventually required, their dosage could be cut to half or less. The most important disadvantage of the technic was the profound respiratory depression resulting from the intravenous injection of the mixture of the two drugs or from phentanyl alone. . . . When necessary, opiate antagonists such as nalorphine effectively counteracted the respiratory depression.

"Another disadvantage was the muscle rigidity involving the thorax and abdominal wall, observed during the induction phase, which resulted in marked resistance to passive inflation of the chest. Intravenously administered

succinylcholine, however, provided effective control. Liver control was not affected by these agents during this investigation. It is concluded that neuroleptanalgesia opens a new approach to the anesthetic management of surgical patients."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

EAMES, G. M. and POOL, K. R. S.: *Clinical trial of oxymorphone in labour.* Brit. M. J. 2:353-355 (August 8) 1964.

"It is said . . . that the ideal obstetric analgesic should have the following properties: (1) relieve pain; (2) not cause foetal asphyxia in effective doses; (3) not alter the course of labour; (4) have a reasonably quick disposal to obviate accumulation. In the search for the ideal drug a clinical trial has been carried out on oxymorphone (Numorphan). . . .

"A pilot trial of 25 unselected cases in labour was carried out to confirm previous reports that it was an effective and safe analgesic. The drug met both these requirements. A double blind trial was then carried out. . . .

"We have been unable to demonstrate that oxymorphone is superior to pethidine when the two are used alone as analgesics in labour. Past experience with drug mixtures—for example, pethidine and phenothiazine—has led to the strong clinical impression that they are more effective as analgesics and sedatives in labour than oxymorphone or pethidine alone. Certainly neither oxymorphone nor pethidine represents the ideal obstetric analgesic."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

FRIEDMAN, A. P.: *Reflection on the problem of headache.* J.A.M.A. 190:445-447 (Nov. 2) 1964.

"At a meeting of the Section on Nervous and Mental Diseases in San Francisco in 1946, Charles Brenner, H. Houston Merritt, and I presented a report on 'The Management of Patients with Chronic Headache.' In the intervening 18 years, some progress has been made in our knowledge about headache—its causes, mechanisms, diagnoses, and treatment. But the intensive study by many investigators has raised more questions than it has answered. . . .

"The current treatment of headache is in part empiric and in part based on what we know of the underlying mechanisms. Treatment of the most common headache syndromes, that is, migraine and muscle-contraction headache, attempts primarily to prevent an attack and alleviate pain. Drugs and psychotherapy are the principal forms of treatment. For headaches in which the pain is initiated by a pathologic process, for example, a cerebral tumor, treatment is directed at the primary process. . . .

"The pertinent facts about drug treatment of chronic, benign headache may be summarized as follows: 1. Whatever drug is used, its effectiveness depends in large part on the patient-physician relation. 2. Few of the many drugs introduced in the past two decades have survived the test of time. 3. The effectiveness of therapy is difficult to appraise accurately, since controlled data are difficult to gather. 4. While controlled double-blind studies are desirable, the results are only as good as the design of the study and the accuracy of the data collected. 5. Any study of drug efficacy must be designed with great care. . . .

"The exact site of origin of a migraine attack remains unknown. Although most experimental studies have been directed to the peripheral nervous system, the central nervous system (CNS) plays an important though incompletely understood role. . . .

"While the problem of the mechanism of migraine is now partly understood, little is known about the etiology. It would appear that migraine does not have one specific etiology but may arise from several causes, and that heredity plays a role in a large number of patients."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

GLESSNER, J. R. and ALLIS, HARRY: *Replacement of injectable with orally administered analgesic agents after surgery.* Anesth. & Analg. 43:356-359 (July-Aug.) 1964.

"The present study was undertaken to determine the feasibility of substituting oral for injectable postoperative medication after the first 24 hours of the postoperative period. Ordinarily, we use meperidine injectable for at least the first 72 hours after major surgery. Oral meperidine has been tried but has never seemed as reliable or as predictable.

"An oral combination of meperidine hydrochloride with promethazine hydrochloride (Mepergan Fortis) was selected because of the frequent assertion that promethazine enhances the action of meperidine and consequently offers the advantages of a lower narcotic dose. This medication was tested blindly against meperidine injections in a novel experiment in which both an injection and a capsule were given to each patient every 4 hours during pain or whenever returning pain brought fresh complaints. The plan provided for shifting of active medication each day the pain endured. . . .

"Only patients undergoing major orthopedic surgery were admitted to the experiment. . . . The 26 patients were unselected as to sex and race; they ranged in age from 13 to 79 years, but debilitated patients were excluded. . . .

"Capsules containing 25 mg. of promethazine hydrochloride with 50 mg. of meperidine were alternated blindly with injections of 100 mg. of meperidine in 26 patients. . . . No significant difference in analgesic efficacy could be found between the two treatment modalities. . . . Combining an adequate amount of promethazine with meperidine permits a greatly reduced dose of the narcotic. The oral preparation can be substituted for meperidine injections and should merit consideration in a wide variety of general clinical applications."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

GOLDMAN, VICTOR and KENNEDY, PAT: *A non-barbiturate intravenous anaesthetic. Report of a pilot trial.* Anaesthesia 19:424-431 (July) 1964.

"An ultra short-acting intravenous agent has recently been introduced for short anaesthetic procedures. This drug is at present under clinical trial in several centres and for research purposes is known as FBA 1420. Unlike most short-acting intravenous anaesthetics introduced to date this agent is not a barbiturate but a phenyloxyacetic acid derivative. . . . It is known chemically as: Propyl

4-(NN-diethyl carbamoyl methoxy)-3-methoxy-phenyl-acetate. It is claimed that this drug possesses the following properties: (1) Rapid onset of action. (2) Analgesic properties. (3) Rapid return of consciousness. A detailed pilot trial was carried out on this drug in order to assess its effectiveness as a short-acting intravenous agent in the dental chair. . . . The total number of cases anaesthetised during this series was 230. . . .

"FBA 1420 does appear to possess some very definite advantages: (1) It is a short-acting intravenous agent. Both recovery and leaving times compare very favourably with other intravenous agents in common use. (2) Recovery from anaesthesia appears very smooth and tranquil with this drug with a marked absence of any "hangover" effects. (3) Hyperventilation is induced with FBA 1420 making blind nasal intubation quite feasible when desired. (4) Very few cases show a drop in blood pressure. (5) It does appear to possess analgesic properties. . . .

"On the other hand there are some decided disadvantages associated with FBA 1420: (1) Viscosity of the solution makes intravenous injection difficult and necessitates the use of a large bore needle for its administration. (2) There appears to be a high incidence of haematomata and the reported case of venous thrombosis is an undesirable factor. (3) There is a higher incidence of hypotension when halothane is used as an adjuvant. (4) Other side effects such as nausea and vomiting seem to occur more frequently with this drug than with other intravenous agents in common use though the absence of hangover effect may account for this."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

HOLTZMANN, LEO, GIBBS, LEON, YUCEOGLU, Y. Z., ABEL, LOUIS, REYES, A. L. and TOLEDO, GREGORY: *Clinical evaluation of propiomazine for preanesthetic medication.* Anesth. & Analg. 43:433-439 (July-Aug.) 1964.

"To obtain a general idea of the ataractic properties of propiomazine, a preliminary study was carried out on 180 adult patients. . . . Encouraged by the preliminary results obtained with this combination, we extended the study, employing the double-blind technic. . . . In this series, which totaled 791 patients ranging in age from 16 to 79 years, the preanesthetic sedation provided by small doses of meperidine combined with propiomazine was compared with the effect of the same doses of meperidine without ataractic. . . .

"The series treated intramuscularly with propiomazine, meperidine, and atropine comprised 393 patients; the controls, treated also intramuscularly with meperidine, atropine, and placebo, numbered 398 patients. Combination of propiomazine in adequate dosage, with a small dose of meperidine and a standard dose of atropine, produced a 26 percent increase in satisfactory results . . . over comparable results obtained in the control series. There were no toxic effects and no instance of definite hypotension or respiratory depression."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

LUNDING, M. and MOLIER, A. G.: *Narcodorm and Brietal. A clinical study utilising a double-blind technique.* Acta anaesth. Scandinav. 8:47-56, 1964.

"Brietal . . . was introduced by Stoelting in 1957. . . . Brietal is an N-methylated barbiturate. . . . As it is not evident from the reports available that Brietal offers any great advantages over Narcodorm (our usually employed barbiturate), we submitted Narcodorm and Brietal to comparative clinical trials. For this purpose we (1) collected the most uniform series of patients possible, (2) avoided premedication with opium derivates, (3) employed a double-blind technique, (4) were only two to induce anaesthesia in all the cases, and (5) used concentrations that are equipotent with regard to anaesthetic action. . . . Our series consisted of (1) patients undergoing minor gynaecological surgery, chiefly dilatation and curettage of the uterine mucosa (D. & C. group) and (2) patients given electro-convulsive therapy (E.C.T. group). . . .

"The series investigated comprised 96 patients undergoing minor gynaecological operations and 48 patients given a total of 336 electro-convulsive treatments. None of the patients were premedicated with opium derivatives. A double-blind technique was employed. In the former group the anaesthetics were supplemented by nitrous oxide and in the latter by suxamethonium chloride. . . .

"By the technique employed the induction dose of Narcodorm was found to be about 2.7 times larger than that of Brietal. There was little difference between Brietal and Narcodorm with regard to the time it took the patients to regain consciousness and orientation. Side effects were most frequent after Brietal, manifested particularly by hiccup and twitchings. After Narcodorm a transitory fall in blood pressure was the most frequent side effect. The side effects were, however, of little importance. Neither the available literature nor the results of the present study afford any grounds for preferring one agent to the other."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

MEAGHER, R. P.: *Methohexital in conjunction with regional anesthesia.* Anesth. & Analg. 43:679-686, (Nov.-Dec.) 1964.

"For total acceptance of regional anesthesia, the patient is usually maintained in a light preoperative sleep or hypnotic state. This has been induced by 'extended' premedication and by parenteral drugs given during the procedure. Both technics can frequently lead to such excessive depression of the cardiovascular and respiratory systems that the physiologic trespass is no longer minimal.

"Recently, an ultrashort-acting oxybarbiturate, methohexital (Brevital) was introduced. . . . Two consecutive series, each composed of 400 cases, were undertaken. The initial series was a double-blind evaluation of the intermittent intravenous infusion of thiamylal (0.6 percent); thiopental (0.6 percent); and methohexital (0.2 percent), in three groups of surgical patients divided according to the regional anesthetic administered. . . . The second series studied the use of a continuous intravenous infusion of methohexital (0.2 percent) in a group of surgical patients divided into three groups according to the regional anesthetic administered, as in the first series. . . .

"Statistical analysis of results using the chi-square test revealed methohexital to be as satisfactory as the two thiobarbiturates studied concerning sedation, quasi-analgesic potency, recovery time, and rate of complications. The major advantages of the methohexital were its ease

of control, lack of severe cardiorespiratory depression, and lack of accumulation."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

MOORE, W. M. O., BROWNE, J. C. M., and HILL, I. D.: *Effect of white sound on pain threshold.* Brit. J. Anaesth. 36:268-271 (May) 1964.

"'White sound' consists of a mixture of sounds of all audible frequencies, and is so called by analogy with white light. It has been claimed that intense acoustic stimulation, using white sound, can reduce or eliminate pain. . . . The effect of white sound on visceral pain produced by contraction of ischaemic muscle has . . . been investigated, using a modification of the method described by Hewer and Keele. . . . Results do not indicate that sound stimulation alters the threshold for pain produced by the contraction of ischaemic muscle. . . . Our experiment has shown no effect while using a wide range of frequencies."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

PARBROOK, G. D. and KENNEDY, B.R.: *Value of premixed nitrous-oxide-and-oxygen mixtures in the relief* of post-operative pain: double-blind trial of 25% nitrous *oxide in oxygen, 15% nitrous oxide in oxygen, and oxygen.* Brit. M. J. 2:1303-1305 (Nov. 21) 1964.

"A previous trial (Parbrook et al., 1964) showed that a 25% nitrous-oxide-in-oxygen mixture had considerable potency for relief of post-operative pain without serious side-effects. To investigate the practicability of its clinical use a double-blind trial was made with varying strengths of the mixture, using apparatus of the type already in routine ward use for oxygen administration. The trial was limited to patients under the age of 60 who were to have upper abdominal operations and who were willing to co-operate in the trial. A series of pain-free volunteers acted as controls. . . .

"In common with the previous trial, in which 25% nitrous oxide was used . . . no untoward side-effects or symptoms were noted in the patients. After completion of the trial it was found that eight of the volunteers had been able to identify the contents of the cylinders subjectively, and three volunteers regarded the 25% nitrous oxide mixture as mildly unpleasant. Four volunteers, however, regarded this mixture as mildly pleasant, while five were unable to identify the mixture or had no special comment to make on this aspect. . . .

"Vital capacity measurments were used to assess relief of post-operative pain after inhaling special premixed nitrous-oxide-and-oxygen mixtures containing 25% nitrous oxide in oxygen and 15% nitrous oxide in oxygen. Oxygen only was used as a control. A series of 12 patients revealed an improvement of vital capacity after 15% nitrous oxide and an even greater improvement after 25% nitrous oxide, whereas a similar series of 12 pain-free volunteers showed no such effect. It is concluded that inhalation of a 25% nitrous-oxide mixture for brief periods can be of value in the early post-operative period."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

PREVOZNIK, S. J. and ECKENHOFF, J. E.: *Phantom sensations during spinal anesthesia.* Anesthesiology 25:767-770 (Nov.-Dec.) 1964.

"The phenomena of the 'phantom limb' syndrome and of 'phantom limb' pain are well documented. However, nowhere can one find a description or an explanation of phantom sensations so commonly observed during spinal anesthesia. . . . The investigation to be reported was undertaken in an effort to seek an explanation for the occurrence of the phantom and to determine its incidence. . . . Spinal anesthesia was administered to 100 successive, unselected patients scheduled for elective lower abdominal, perineal or extremity surgical procedures. . . .

"Twenty-four of the 100 patients experienced a painless phantom sensation which persisted throughout the motor blockade, and disappeared as motion returned. The phantoms perceived were directly related to the position of the lower extremities at the time of onset of motor paralysis. Patients in whom motor block began with lower extremities raised as for a leg or perineal sterile preparation felt as though their legs continued to be elevated even after they had been returned to the supine position. . . .

"Fifteen patients who were to have lower extremity surgical procedures were included in this series. Six did not have their legs elevated until after motor paralysis was complete and none experienced phantoms. The nine remaining patients had their legs elevated before motor paralysis was complete and all perceived an 'elevated leg' phantom that persisted for the duration of the motor paralysis.

"Patients put in the lithotomy position prior to motor blockade felt as if their knees remained flexed after return to the supine position until motor power returned. . . . The remaining four phantoms were reported by those patients staying in the lateral decubitus position after the subarachnoid injection. Two patients perceived their feet as turned laterally and the remaining two as if their thighs were flexed on the abdomen. . . .

"Seventy-three patients were in the dorsal recumbent position with legs outstretched at the time of the onset of motor blockade, did not experience phantoms and exhibited a complete loss of proprioceptive function. Three patients given a saddle block spinal did not lose motor or proprioceptive function and failed to experience phantoms."

From LUNDY, J. S., and MC QUILLEN, F. A.: Anesthesia Abstracts. Minneapolis: Burgess Publishing Co., 1965, vol. 64. Copyright by J. S. Lundy.

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Book Reviews . . .

Infectious Disease of Children, Third Edition

by SAUL KRUGMAN *and* ROBERT WARD, *423 pp., ill., C. V. Mosby Company, St. Louis, 1964. $15.75*

The majority of physicians are called upon to diagnose and treat infectious diseases a number of times each day in their practice. The authors have written a book which, in my opinion, is unexcelled in bringing current information to the reader concerning all such diseases.

Of all infectious diseases those of the respiratory tract are the most common. Chapters 16 and 17 take up etiology, diagnosis, and treatment of acute respiratory tract infections. According to the authors, it has been estimated that over 90% of such infections are caused by nonbacterial agents, most of which are not susceptible to antibiotic therapy. There are now over 60 viruses known to cause respiratory diseases in man. The most important cause of lower respiratory tract infections in children is the recently recognized respiratory syncytial virus (RS). Parainfluenza viruses may cause croup and may contribute to other respiratory tract infections, both mild and severe. Adenoviruses are responsible for a small percentage of respiratory illnesses. Influenza viruses cause widespread epidemics, but only a small percentage of day-to-day illnesses. Picornaviruses include the newly discovered rhinoviruses and the enteroviruses (polio virus, coxsackie virus, and echo virus) which may all give rise to respiratory illness, although poliovirus is not usually considered as a source of significant throat or respiratory infections. Rhinoviruses have been recently isolated, and have been shown to cause common colds in both adults and children. Reoviruses are a newly isolated group which may be proved pathogenic for man as well as animals. Herpes simplex virus, varicella virus, and cytomegalovirus have many properties in common; all may cause respiratory illness at times. Psittacosis virus is one of a group of large viruses which may spread from birds to man with resultant acute pneumonitis. Lymphocytic choriomeningitis virus may spread from certain animals to man, giving rise to respiratory illness. Mycoplasma pneumoniae (Eaton Agent, PPLO) may cause atypical pneumonia which responds to antibiotic therapy. Q fever, caused by Rickettsia burneti, may give rise to atypical pneumonia. Among bacteria chiefly responsible for respiratory disease are group A hemolytic streptococcus, staphylococcus, pneumococcus, and H. influenzae. Differential diagnosis is difficult and sometimes impossible on clinical grounds, and at times even with cultures and viral studies. The authors make a plea, however, for avoiding antibiotic treatment in patients whose signs and symptoms point to viral disease, while at the same time warning of the dangers of bacterial complications.

A chapter of considerable value to the practitioner is the one on rabies. How frequently we are confronted with the necessity to make a decision whether or not to give rabies vaccine. The authors give specific recommendations concerning the indications for, and dosages of, vaccine and hyperimmune serum, as well as local treatment of wounds. Preventive and control measures are also presented in some detail.

An effective method is used of grouping enteroviral infections in one chapter. These include polio viruses, coxsackie viruses, and echo viruses, which have many similarities. There are 58 members of the enterovirus family known at the present time. There are both similarities and differences in symptomatology in the individual viruses and types. All of them are capable of causing central nervous system and intestinal involvement, but they vary in severity. Skin rashes and respiratory illness or both may result from coxsackie virus or echo virus infection depending on the virus, the type, and the host response. All factors are thoroughly presented.

Obviously, in a review such as this, one can only mention a few salient points concerning the book. The authors are especially well qualified to write such a book. Dr. Krugman is professor and chairman of the Department of Pediatrics, New York University School of Medicine. Dr. Ward is professor and chairman of the Department of Pediatrics, University of Southern California School of Medicine. He was formerly professor and head of pediatrics at New York University. Both men are widely known as teachers and clinicians, as well as for their viral research.

LAURENCE G. PRAY, M.D.
Fargo

Hernia

edited by LLOYD M. NYHUS *and* HENRY N. HARKINS, *836 pp., ill., J. B. Lippincott Co., Philadelphia, 1964. $28.50*

This monograph on hernia is a most comprehensive volume based on the surgical experience of Drs. Nyhus and Harkins and the contributions of 103 world-recognized authorities. The material is presented in a clear, detailed, and documented manner and is developed under the following sections: groin hernia, ventral hernia, diaphragmatic hernia, internal hernia, pelvic hernia, and a section on the consideration of general aids to repair.

The historical survey of the treatment of inguinal hernia should be interesting and educational to the young surgeon as well as to the most knowledgeable surgeon. The book is generously illustrated with photographs, excellent detailed drawings, and sketches which aid materially in the presentation of the subject. The illustrations are of high quality.

The editors have utilized a very interesting feature in inviting an expert to furnish comments on the subject which was presented in the chapter. The commentator in some instances amplified favorably on the subject and in other instances expressed dissimilar opinions. These "Special Comments" were stimulating and pointed up that there is still some controversy in the anatomical consideration and technical surgical care of herniae. At the end of each chapter there is the "Editorial Comment" made by either one of the editors and, in some instances, by both of the editors. This feature makes for a worthwhile educational discussion which is fairly presented.

The references are well selected for the subject matter that is presented and serve as an excellent source of bibliographic material. The bibliographic index and the subject index are well detailed. The appendix compiles a list of books on hernia which the editors consider to be

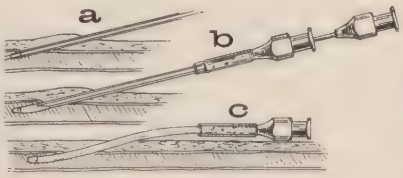
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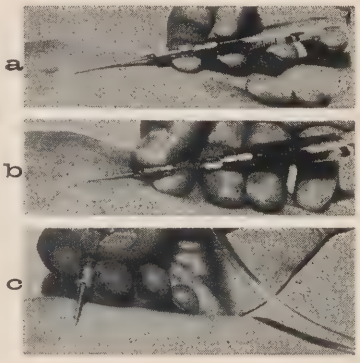
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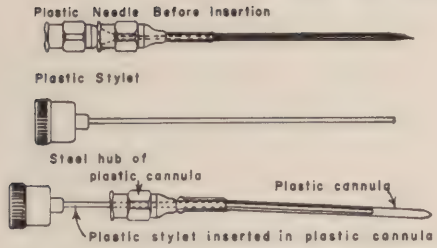




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(Continued from page 12A)

the best works on the subject. The format of the printed page is in two columns which makes for easy readability.

This book contains an abundance of pertinent information on all phases of hernia which has been compiled in an exacting manner by Drs. Nyhus and Harkins. The subject of hernia in this volume is presented in the best surgical opinion of the current period. The monograph will be a surgical landmark and it is recommended without reservation to all those who have an interest in hernia, be he starting his surgical career or a master surgeon.

ERNEST R. ANDERSON, M.D.
Minneapolis

Pulmonary Embolic Disease

edited by ARTHUR A. SASHARA, M.D., *and* MYRON STEIN, M.D., *312 pp., ill., Grune & Stratton, Inc., New York, 1965. $14.50*

This comprehensive monograph presents the proceedings of the Symposium on Pulmonary Embolic Disease held in Boston, May 22 to 23, 1964. Forty-three individual clinicians and basic scientists contribute presentations to this book which has been carefully edited by the authors.

The text is divided into 4 sections, each comprised of 6 to 8 presentations, and each section is concluded by a discussion of the individual papers by other symposium participants. The first section on "Basic Science" contains information on blood clotting, the pathophysiology of thrombus formation, and the pharmacology of anticoagulant drugs. The second section on "Experimental and Clinical Thromboembolism" presents pathological and hemodynamic observations, pulmonary function data, and a great deal of basic cardiopulmonary pathophysiology, as well as a discussion of serum enzyme diagnosis of pulmonary embolism. The third section is concerned with "Graphic Methods" and contains papers on electrocardiography, vectorcardiography, radiology, angiography, and radioisotope scanning in pulmonary embolism and infarction. The final section is on "Clinical Aspects" and contains a wealth of historical and clinical information, including good discussions of anticoagulant therapy and prophylaxis, venous ligation, and pulmonary embolectomy.

A monograph is usually a treatise on a single subject by a single author. This monograph is by 43 authors, so the reader is subjected to 43 varying styles of presentation in a kaleidoscopic manner which almost leaves him breathless. This form of presentation precludes the smooth flow of writing which draws the reader along from chapter to chapter and presents abrupt transitions in subject matter. A reader may find more than he wishes to know about a certain aspect of thromboembolic disease and less about another. It is perhaps a symptom of the "information explosion" that 43 contributors have to write a monograph.

The value of the book, however, rests in the depth and accuracy of each presentation which would simply not be possible for any one person to contribute, and this value far outweighs the disadvantages of the symposium method of presentation.

The editors have done an excellent job of arranging the presentations and an amazingly competent job of editing and, above all, have provided an index to find one's way back to specific points. The quality of the photographs, X-ray reproductions, graphs, and charts is superior throughout. The book is highly recommended for the internist, thoracologist, thoracic surgeon, and appropriate basic scientists and belongs in the library of every medical school, clinic, and hospital, available to medical students and house staff.

WILLIAM R. FIFER, M.D.
Minneapolis

An Introduction to Electrocardiography

by THOMAS M. BLAKE, M.D., *143 pp., ill., Appleton-Century-Crofts, New York City, 1964. $4.95 (paper back)*

The book is mainly for the third year medical student and can be recommended for that level of medical education. It has a fluidly written and simple introduction and can be recommended also for medical technicians and nurses. The book is not meant as guide for actual electrocardiograph interpretation but may well stimulate the interest to read some more comprehensive primer or textbook of electrocardiography. The main types of abnormalities are explained, and it is an advantage that aspects of spatial vectorcardiography are included as basis for explanation of the conventional electrocardiograph.

There are several statements to which the reviewer takes exception. For instance: "With experience one learns the normal and can recognize deviations from it." Recognition of normality should not depend on the individual experience of the electrocardiographer, but on statistically analyzed distributions of electrocardiograph items in healthy population. The large normal variability of the electrocardiograph is not discussed, but without it, abnormal changes cannot be safely recognized. On the same page, the author writes that "A concept of the relationship of the components of the tracing, though, as discussed so far in their frontal projection, will go far to minimize the need for statistics and guess work and will help put electrocardiography on a more rational basis." The author does not seem to be aware that only on the basis of statistical evaluation a reliable electrocardiograph interpretation is possible. Minimizing the need for statistics means actually emphasizing guesswork.

It is surprising that Lepeschkin's QX:QT ratio is described as the most important criterion for an abnormal exercise test. The author should have been aware that this criterion is highly controversial, to say the least.

ERNST SIMONSON, M.D.
Minneapolis

Stereoscopic Manual of the Ocular Fundus in Local and Systemic Disease

by FREDERICK C. BLODI *and* LEE ALLEN, *132 pp., ill., C. V. Mosby Co., St. Louis, Mo., 1964. $32.50*

This beautiful manual, with its memorable stereoscopic transparencies, is a fine addition to the library of any physician. There are over one hundred stereo transparencies, ranging from the normal fundus with its variations, to senile changes, with all forms of retinal disease between. The photos are of excellent quality and the stereoscopic effect gives a feeling of reality to their perusal. Since so much disease of the retina, vitreous, and disk involves elevation from the posterior pole of the eye, the stereo views are of decided value.

Each photograph has an accompanying case history describing the patient, the course of the ocular disease, and the pathology seen in the slide. The well written text then briefly elaborates on the disease under study so

(Continued on page 18A)

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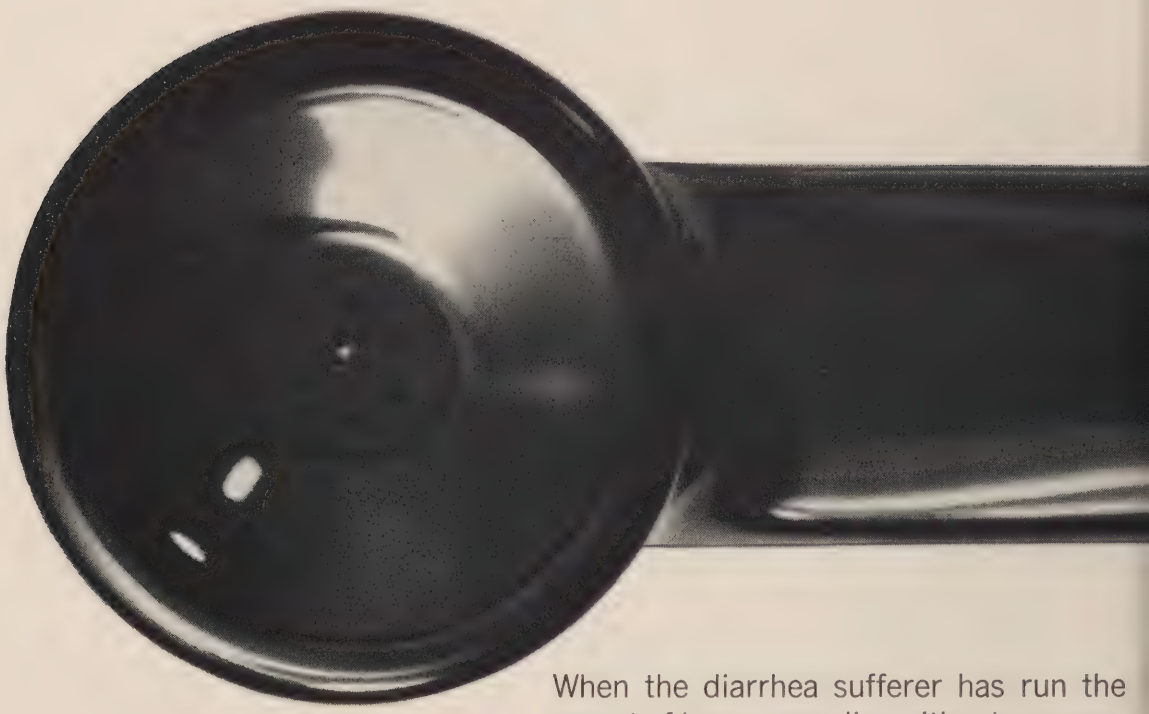
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min K. Neomycin: Patient should be observed for new infections due to bacteria or fungi. *Side Effects:* Sulfonamide: Sensitivity reactions may occur (e.g., skin rashes, anemia, polyneuritis, fever; agranulocytosis with a fatal outcome has been reported). Reduction of thiamine output in the feces and of vitamin K synthesis has been observed. Neomycin: Nausea, loose stools possible.

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(Continued from page 14A)

that, quite painlessly, in the course of a few slides, a fairly good mental impression of the disease can be obtained. Photomicrographs give still another detail of the disease process and further elaborate on the pathology under study.

This is a text which takes the reader by the hand through the forests of retinal disease. The diseases presented are in their full-blown manifestations and are readily recognizable. One of the possibly unexpected effects of this book is that it arouses the desire to see more retinal disease and to see it in actuality, through a dilated pupil.

This is a book enthusiastically recommended to all.

FREDERICK C. WUEST, M.D.
Minneapolis

Leukemia

by WILLIAM DAMASHEK, M.D., *and* FREDERICK GUNZ, M.D., *2nd. ed., 594 pp., ill., Grune & Stratton, New York City, 1964. $25*

This second edition successfully integrates the more recent knowledge about leukemia with the vast wealth of material presented in the 1958 edition. Claiming to be neither an encyclopedia nor a textbook, it serves effectively as the latter, and in covering the field of human leukemia thoroughly, it is virtually encyclopedic in scope. Established knowledge about leukemia is covered exhaustively and many of the newer developments are explored and assessed, including such topics as the relation of viruses to leukemia, chromosomal studies in leukemia (significance of the Ph 1 chromosome and the trisomy syndromes involving the G 21 chromosome), and results of recent cytogenetic and cytochemical methods.

In addition to consideration of acute and chronic leukemia, the clinical discussion includes a section on multiple myeloma and macroglobulinemia, which the authors consider as neoplastic proliferations of immunologically competent cells. The relationships between immunologic and neoplastic proliferations are discussed further in the new section on lymphoproliferative disorders. This chapter contains much interesting speculation about functions of the lymphoid system and complements the section on myeloproliferative disorders which precedes it in the text.

Dr. Dameshek's concept of myeloproliferative disorders is particularly well presented, a reflection of his long-standing interest and study of these seemingly related conditions. Included is an enlightening discussion of the diGuglielmo syndrome which takes some of the confusion out of that complex group of conditions.

Sections on treatment are fairly didactic and give extensive evaluations of the drugs in current use, up to and including vincristine sulfate (Oncovin®) and the present alternative treatment programs. One might hope for somewhat more specific recommendations, (sequential or cyclic therapy in acute leukemia, for example) but it is recognized that many of the questions can't be entirely settled by rigid formulation in view of constantly changing programs and reported results.

The material is presented in the characteristically clear and easily read prose style of Dr. Dameshek and his collaborator, Dr. Gunz. Dr. Gunz, formerly a research fellow in hematology at the New England Center Hospital, is now doing clinical and basic research studies in

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hematology and cytogenetics in Christ Church, New Zealand, and publishes extensively in the foreign and American literature.

The review of this book would be incomplete without comment on the bibliography which appears at the end of each section. These are lengthy and complete with a thousand new references appearing for the first time in this edition alone. The volume is highly recommended to all clinicians and pathologists who have an interest in leukemia.

ROBERT A. GREEN, M.D.
Minneapolis

Human Reproduction and Sexual Behavior

edited by CHARLES W. LLOYD, M.D., *564 pp., ill. Lea & Febiger, Philadelphia, 1964. $12.50*

This is a beautiful book, beautifully illustrated and well written. The foreword is by George W. Corner, a great man who has spent his life studying in this field. As he says, "Our profession has been able to solve some of the most intricate riddles in medical diagnosis, and to perform almost incredible feats of surgical skill, but it has long been baffled by commonly occurring deviations and malfunctionings of mind and body in the realm of sex behavior, and in the functioning of the reproductive system."

As Dr. Corner goes on to say, the physical phenomena underlying sex physiology and behavior have been poorly understood. The phenomena in man and in the higher animals are not similar enough so that much can be learned from a study of comparative physiology. For instance, "the external manifestations of the human female reproductive cycle are apparently so different from those of infra-primate animals that, once the problem became apparent, it took two generations of observation and experiment to discover the basic similarity of these phenomena." Another difficulty, of course, is the complexity of the human psyche as it is influenced by sexual factors—factors which cannot be studied experimentally. Worse yet, many men have always been very reluctant to discuss sexual matters. "Such prudery fortunately did not forbid, though it often hampered, strictly physical diagnosis and treatment in gynecological conditions and in obstetrics, but it did most assuredly deter medical men from discussing with their patients, and from studying mental and behavioral anomalies that were sometimes more injurious and distressing than physical lesions of the genital organs."

Very important was the publication, in 1932, of the book edited by Edgar Allen on "Sex and Internal Secretions." Here was a great beginning and a great landmark. Now, as Dr. Corner says, in 1964 Dr. Charles W. Lloyd and fifteen collaborators have published a work which may confidently be expected to become another landmark, this time for those who are working with patients rather than animals or chemicals in a laboratory.

"This book is unique in bringing together, in one volume, summaries of what is known today about all the functional elements of sex behavior and reproduction—endocrine, neurological, psychological, and psychiatric. It indicates the pathways by which we may hope to make further advances in this important field."

WALTER C. ALVAREZ, M.D.
Chicago

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News Briefs . . .

North Dakota

DR. DENNIS E. WOLF has opened practice in the Richardton Medical Clinic in association with Dr. Henry F. Slolminski. Dr. Wolf received his medical degree in 1962 from the University of Wisconsin.

* * * *

DR. WILMER G. GARRETT, Bismarck, has been elected chairman of the recently established outpatient pulmonary diagnostic treatment center at St. Alexius Hospital, Bismarck. Dr. Ralph J. Dunningan, also of Bismarck, has been elected vice-chairman.

* * * *

DR. GEORGE M. JOHNSON, pediatrician, is a new member of the staff of the Missouri Valley Clinic, Bismarck. Dr. Johnson graduated in 1960 from the University of Washington School of Medicine, Seattle.

* * * *

DR. ROBERT L. LEEGARD has joined the staff of the Fargo Clinic in the department of anesthesiology. He graduated in 1962 from the Temple University School of Medicine, Philadelphia.

* * * *

DRS. MARK T. MATHEWS and GERALD J. DORFF have been assigned to duty at the Public Health Service Hospital in Belcourt. Dr. Mathews received his medical degree in 1964 from Loma Linda University, Loma Linda, California, and Dr. Dorff received his from Marquette University, also in 1964.

* * * *

DR. DELBERT J. HLAVINKA has started practice in Mayville as a member of the Mayville Clinic. Dr. Hlavinka graduated in 1961 from the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, N.C. He has been practicing medicine at Mott for the past three years.

* * * *

DR. HAAKON CARLSON has joined the Hazen Clinic. Dr. Carlson, a native of New Town, received his medical degree at the University of Wisconsin, Madison, and recently completed his internship at St. Mary's Hospital, Duluth.

* * * *

DR. RICHARD H. SEIFERT, Fargo urologist, has ben certified by the American Board of Urology. Dr. Seifert received his medical degree in 1957 from the Stritch School of Medicine of Loyola University, Chicago.

* * * *

DR. GERALD T. SAILER, a native of Hazen, has joined the Hettinger Clinic. Dr. Sailer received his medical degree from Baylor University, Houston, in 1961. For the past two years he has been medical health officer in charge of the U.S. Public Health Service Hospital at Belcourt.

* * * *

DR. DONALD J. STRAND, a native of Mandan, has been appointed a medical defense hospital consultant in the New York State Health Department. Dr. Strand received his medical degree in 1946 from Temple University, Philadelphia.

* * * *

DRS. RODNEY O. SLONIM and BERNIE ZITSOW, both of Winnipeg, Manitoba, have joined the Mahoney-Lazareck Clinic, Devils Lake.

THREE PHYSICIANS HAVE BEEN APPOINTED to the State Board of Medical Examiners, all for three-year terms. Renamed to second terms were Dr. Joseph W. Cleary, Bismarck, and Dr. Arthur C. Fortner, Fargo. Dr. Amos R. Gilsdorf, Dickinson, was appointed to succeed Dr. Henry L. Reichert, Dickinson, who had served the maximum two consecutive terms allowed by law.

* * * *

DR. LESTER S. FROGNER, 62, has retired after twenty-seven years with the Veterans Administration. Dr. Frogner graduated from the University of Minnesota Medical School in 1933. He was admitting physician at the Fargo VA Center from 1948 to his retirement.

* * * *

DR. KENNETH J. JOHNSON, internist with the Quain and Ramstad Clinic in Bismarck, has an article in a volume called "The Mast Cells." The book is a collection of 2,500 articles on cells and food allergies selected by Dr. Hans Selye from 8,500 papers on the subject published in the past one hundred years.

* * * *

DR. ALBERT H. FORTMAN of the Capital City Clinic, Bismarck, has been certified as a diplomate of the American Board of Surgery. Dr. Fortman graduated in 1954 from the Northwestern University Medical School, Chicago. He is a member of the surgical staffs of St. Alexius, Bismarck, and Mandan hospitals.

* * * *

DR. PAUL R. VANDERSTEEN has been appointed to the staff of the Medical Arts Clinic, Minot. A native of St. Paul, Dr. Vandersteen received his medical degree in 1962 from the University of Minnesota.

* * * *

MEETINGS, 1965-66

October, 1965

1- 2	North Dakota Easter Seal Society, Bismarck
12-14	North Dakota State Nurses Association, Minot
19-20	North Dakota Hospital Association, Fargo
20-22	North Dakota Rehabilitation Association, Bismarck
30	Quain & Ramstad Clinic's Fall Clinical Conference, Bismarck
30	Woman's Auxiliary Fall Board Meeting, Bismarck

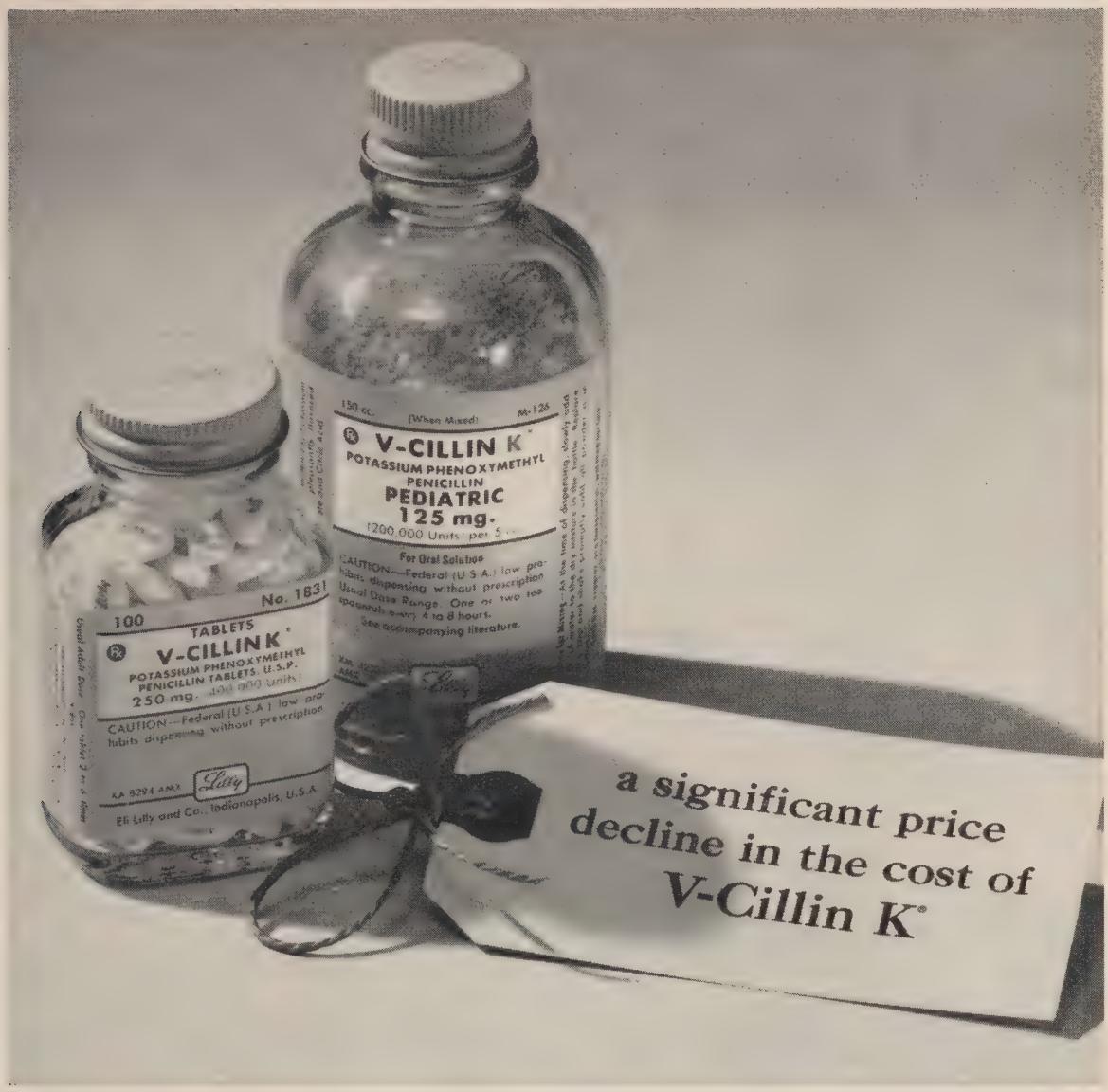
November, 1965

3	North Dakota Mental Health Association, Fargo
6- 7	North Central Medical Conference, Minneapolis
19-20	North Dakota Chapter, American Academy of General Practice, Dickinson
20	North Dakota Physicians Service Board of Directors (tentative)
28-Dec. 1	American Medical Association Clinical Convention, Philadelphia

Minnesota

DR. C. ALLEN GOOD, head of a section of diagnostic roentgenology at the Mayo Clinic and professor of radiology at the Mayo Graduate School of Medicine, University of Minnesota, has been elected president of the American Board of Radiology.

(Continued on page 22A)



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Contraindications and Precautions: Although sensitivity reactions are much less common after oral than after parenteral administration, V-Cillin K should not be administered to patients with a history of allergy to penicillin. As with any antibiotic, observation for overgrowth of nonsusceptible organisms during treatment is important.

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Additional information available to physicians upon request. Eli Lilly and Company, Indianapolis, Indiana.

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NEWS BRIEFS

(Continued from page 20A)

DR. JAMES C. CAIN, gastroenterologist at the Mayo Clinic, has been named by President Lyndon B. Johnson to be chairman of the National Advisory Committee on Selective Service. Dr. Cain, a Texan, has known President Johnson since before his political days and examined the President in Washington and in Rochester following Mr. Johnson's 1956 heart seizure.

* * * *

DR. THADDEUS J. LELWICA, a native of Winona and a 1960 graduate of the University of Minnesota, has begun practice in the Lakewood Clinic, Staples.

* * * *

DR. RAMON MENDIOLA, general surgeon, has joined the staff of the Lakeview Clinic, Waconia. Dr. Mendiola graduated in 1955 from the University of Santo Tomas Faculty of Medicine and Surgery, Manila, and completed training in surgery at Mount Sinai Hospital, Minneapolis, and Ancker Hospital, St. Paul.

* * * *

DR. FRANK R. KOTCHEVAR, 66, has retired from the East Range Clinic, Eveleth, with which he has been associated since 1928. Dr. Kotchevar graduated in 1928 from Northwestern University Medical School, Chicago, and is a member of the American College of Surgeons.

* * * *

DR. LEON H. FLANCHER, 76, has resigned as superintendent and medical director of Sunnyrest Sanatorium, Crookston, concluding a career of more than fifty years devoted to study and treatment of tuberculosis. Dr. Flancher graduated from Milwaukee Medical College in 1910 and received the degree of Master of Public Health from the University of Minnesota in 1943. He is a member of the American Thoracic Society and of the American College of Preventive Medicine.

* * * *

DR. CHARLES F. CODE, physiologist at the Mayo Clinic, has been appointed director for medical education and research of the Mayo Foundation. Dr. Code will work with Dr. Victor Johnson, director of the Mayo graduate school of medicine, who will retire next April.

* * * *

DR. ADRIAN L. KAPSNER has resigned from the Hutchinson Medical Center to accept a position as resident in radiology with the Veterans Administration Hospital, Minneapolis.

* * * *

DR. HARTVIG B. ROHOLT has opened an office for the practice of internal medicine and diagnosis in the Center Arcade Building, Bemidji. Dr. Roholt, a 1946 graduate of the University of Minnesota, was associated with the Bemidji Clinic for the past year.

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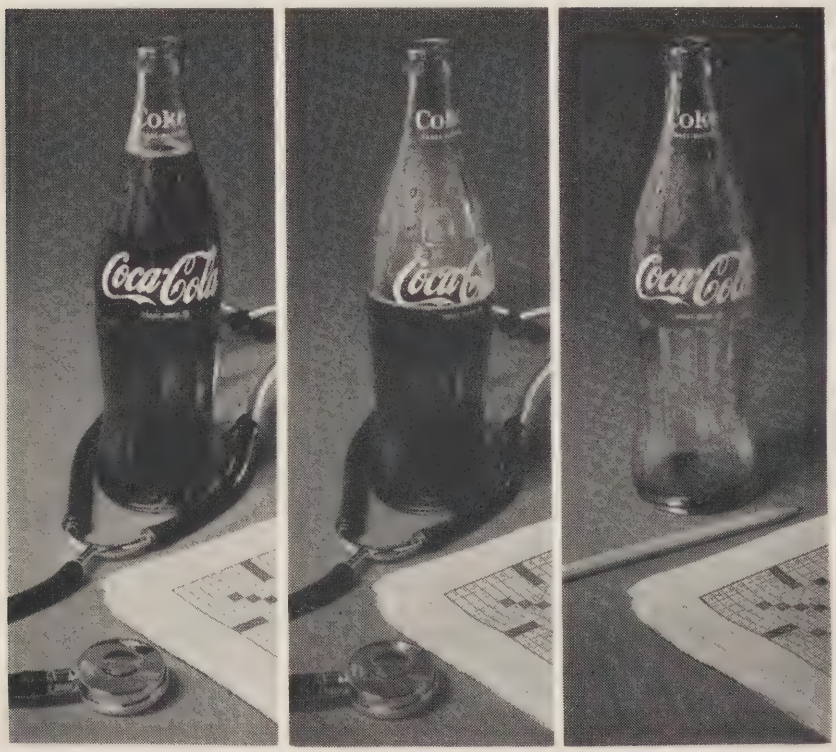
DR. JACK A. NAROS, recently of Big Fork, has established regular office hours at the Crosby Clinic to succeed Dr. Richard T. Henry who has accepted a medical position in Florida. Dr. Naros received his medical degree from the University of Minnesota in 1957.

* * * *

DR. THOMAS G. BIRKEY has joined the staff of the Montivideo Clinic. Dr. Birkey is a native of Minneapolis and a 1962 graduate of the University of Minnesota Medical School. He is a member of the American Academy of General Practice.

* * * *

DR. JOEL O. BRENDE, Minneapolis physician, is serving a two-month mission in New Guinea under the auspices of the World Brotherhood Exchange. He will return to Minneapolis the latter part of November.



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NEWS BRIEFS

DR. FREDERICK C. WUEST, ophthalmologist, has begun practice in the Wayzata Medical Building, Wayzata. Dr. Wuest received his medical degree in 1956 from New York Medical College.

* * * *

DR. CHARLES A. TIETZ has joined the staff of the Lenont-Peterson Clinic, Virginia. Dr. Tietz, a 1961 graduate of the University of Chicago School of Medicine, will specialize in obstetrics and gynecology.

* * * *

DR. DAVID G. SMITH, a native of Minneapolis, has begun practice as a member of the Watertown Medical Clinic. He received his medical degree from the University of Minnesota in 1962.

* * * *

DR. OVE A. ERDAL, Albert Lea general practitioner and gynecologist, has moved to Moscow, Idaho. He practiced in Albert Lea for the past eighteen years.

* * * *

DR. WILLIAM H. STEWART, former resident of Minneapolis, has been named director of the National Heart Institute, succeeding Dr. Ralph E. Knutti, who has retired. Dr. Stewart received his medical degree from Louisiana State University in 1945.

* * * *

DR. HOWARD M. LEVINE, Minneapolis gynecologist, has been certified a diplomate of the American Board of Obstetrics and Gynecology. Dr. Levine is a 1957 graduate of the University of Louisville School of Medicine.

* * * *

DR. MAURICE B. VISSCHER, head of the physiology department at the University of Minnesota, has been elected president of the National Society for Medical Research. Dr. Visscher succeeds Dr. Hiram E. Essex, a member of the staff of Mayo Clinic, Rochester.

* * * *

DR. CECIL J. WATSON, head of the department of medicine at the University of Minnesota Medical School since 1943, has been appointed director of medical education at Northwestern Hospital, Minneapolis. Dr. Watson will continue to hold his appointment as professor of medicine at the University.

* * * *

DR. FREDERICK D. BANFIELD has become associated with the Olmsted Medical Group, Rochester, as a general practitioner. Dr. Banfield received his medical degree in 1962 from Temple University, Philadelphia.

* * * *

DR. MILTON N. ALTER of the department of neurology of the University of Minnesota has received a grant of $15,000 to study methods of diagnosis of mentally retarded individuals. The grant was made by the U.S. Public Health Service.

* * * *

DR. JOHN P. SAVARYN, general surgeon, has reopened medical practice in Waconia after completing a four-year fellowship in surgery at the University of Minnesota. Dr. Savaryn received his medical degree in 1951 from the Johann-Wolfgang-Goethe-Universitat Medizinische Fakultat, Frankfurt-am-Main, Prussia.

* * * *

DR. CLIFFORD PESONEN has joined the Austin Clinic as a member of the department of general medicine. Dr. Pesonen received his medical degree from the University of Minnesota in 1963.

(Continued on page 24A)

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FREE PARKING

(Continued from page 23A)

DR. DONALD S. ASP, a native of Milaca, has joined the Parkers Prairie Clinic. Dr. Asp graduated from the University of Minnesota School of Medicine in 1964 and interned at Bethesda Lutheran Hospital, St. Paul.

* * * *

DR. RICHARD D. LUNDBORG, a native of Milan and a graduate of the University of Minnesota Medical School, has been appointed to the staff of the Mayo Clinic as a consultant in anesthesiology.

South Dakota

DR. JOHN W. STEWART has joined the staff of the Homestake Hospital, Lead. Dr. Stewart graduated from the University of Minnesota Medical School and recently completed his internship at the Detroit Receiving Hospital, Detroit, Mich.

* * * *

DR. WALTER A. KITZLER, general surgeon, has joined the staff of the Webster Clinic, Webster. Dr. Kitzler has been practicing at Faulkton the past two years.

* * * *

DR. BRUNO E. STRAUSS has reopened an office for the general practice of medicine in the Parker Medical Building, Parker, following training in radiology at the University of Washington, Seattle.

* * * *

DR. WALTER C. MILLER, pediatrician, has joined the Aberdeen Medical Center. He graduated in 1962 from the Stritch School of Medicine of Loyola University, Chicago.

* * * *

DR. DONALD H. LINDEMAN has begun the general practice of medicine at the Viborg Clinic. Dr. Lindeman graduated in 1962 from the University of Nebraska College of Medicine, Omaha.

* * * *

DR. JUAN R. CHAVIER, pediatrician, has joined Dr. Noel de Dianous in practice at Aberdeen. Dr. Chavier has just completed his residency in pediatrics at the Children's Hospital of Ohio State University, Columbus.

* * * *

DR. DONALD K. FABER, general surgeon, has opened practice in Lennox after having been in practice in Sioux Falls since 1963. He received his medical degree from the State University of Iowa in 1959.

* * * *

DR. JAMES E. RYAN has joined the Spiry Clinic, Mobridge. Dr. Ryan is a native of South Dakota and a graduate of the University of Nebraska Medical School.

* * * *

DR. JAMES K. JACKSON, orthopedic surgeon, has become associated with the Yankton Clinic. Dr. Jackson received his medical degree from the State University of Iowa College of Medicine in 1958. He has just completed a three-year residency in orthopedic surgery at Nebraska Orthopedic Hospital, Lincoln.

* * * *

DR. CLARENCE J. KOOIKER has been appointed acting medical officer at Sioux Sanatorium, Rapid City, replacing Dr. Everrett A. King, who will retire from the U.S. Public Health Service in November after twenty-four years of service. Dr. Kooiker, a radiologist, has been chief of the X-ray department of the PHS Hospital in New Orleans for the past two years.

(Deaths on page 26A)

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Anturane, brand of sulfinpyrazone, is available as white, scored tablets of 100 mg. Initially, give half a tablet 4 times daily with meals or milk, increasing in one week to one tablet q.i.d. Increase to two tablets q.i.d. if necessary, and reduce if possible to as low as half a tablet q.i.d. after control. Continue through acute attacks, which can be concomitantly treated with phenylbutazone.

Patients on other uricosurics may be transferred to this drug at full dosage.

Contraindications
Active peptic ulcer. Salicylates and citrates antagonize the drug's action and are contraindicated for concomitant use.

Warning
Use with caution in pregnant women.

Precautions
Keep patients under close supervision and make periodic blood counts. Use cautiously in patients sensitive to pyrazoles, in patients with histories of peptic ulcer, and in conjunction with sulfa drugs, the sulfonylurea hypoglycemic agents, and insulin, the actions of which may be potentiated.

In mobilizing urate deposits, the drug may precipitate acute attacks of gout, urolithiasis, and renal colic, especially in the initial stages of therapy. Ensure adequate fluid intake and alkalinize the urine. With renal impairment, test renal function periodically.

Adverse Reactions
The most frequent are upper gastrointestinal disturbances. The drug may activate peptic ulcer. Rash occurs infrequently. Although not reported to date, blood dyscrasias are a possibility.

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in gout



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"the most effective and best tolerated of the currently available uricosuric agents for the control of gout."*

Anturane, brand of sulfinpyrazone, was developed in the Geigy laboratories. Its pharmacologic activity is limited almost exclusively to increasing the urinary excretion of uric acid. For this reason, it is a drug of choice in chronic tophaceous gout and acute intermittent gout. It is not intended for relief of acute attacks of gout.

In most patients, the drug rapidly reduces serum uric acid levels to normal. This not only prevents new tophi but also mobilizes and promotes the excretion of urates already in the tissues. The reduction of tophi and periarticular crystals results in more mobile, less painful joints.

Anturane, brand of sulfinpyrazone, materially reduces the number and severity of acute attacks of gout. It may also be used to counteract hyperuricemia induced by certain diuretics.

Because of its potency, the drug is often effective in patients refractory to other uricosuric agents. Patients can usually be maintained indefinitely on it without cumulative effects or development of tolerance.

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*Kuzell, W. C., et al.: Effect of sulfinpyrazone on serum uric acid in gout: a long-term study, Geriatrics 19:894, 1964.

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Deaths . . .

DR. JOSEPH F. MALLOY, 68, of Leola, S.D., died July 29. Dr. Malloy, urologist and general practitioner, graduated in 1921 from Creighton University School of Medicine, Omaha. He was a member of the American College of Surgeons.

* * * *

DR. ROY T. MILLER, 39, former St. Paul resident, died Aug. 7 in Walnut Creek, Calif. Dr. Miller was a radiologist and a 1950 graduate of the University of Minnesota Medical School. He was a member of the American College of Radiology.

* * * *

DR. DANIEL W. MATTHAEI, 83, of Fessenden, N.D., died July 17. Dr. Matthaei received his medical degree in 1909 from the University of Illinois, Chicago.

* * * *

DR. MYRON LYSNE, 60, Minneapolis physician, died Aug. 15 while boating near Fort Frances, Ontario. Dr. Lysne was a 1936 graduate of the University of Minnesota, and a member of the American Academy of General Practice.

* * * *

DR. FRED Z. HAVENS, 75, emeritus plastic surgeon of the Mayo Clinic staff, died July 29 in Rochester following a heart attack. Dr. Havens received his medical degree in 1915 from Rush Medical College, Chicago. He was a member of the American Academy of Ophthalmology and Otolaryngology, the American Association of Plastic Surgeons, the American Laryngological Association, the American Laryngology, Rhinology, and Otology Society, and the American Society of Plastic and Reconstructive Surgery.

* * * *

DR. FREDERICK W. HOFFBAUER, 54, chief of medicine of Hennepin County General Hospital, died July 30 in Minneapolis. Dr. Hoffbauer, an internist, graduated in 1937 from the University of Minnesota Medical School. He was a member of the Central Society for Clinical Research, the American College of Physicians, the American Society for Clinical Investigation, and the American Society for Experimental Pathology.

* * * *

DR. DAVID B. PETERSON, 64, of St. Paul, died in his home July 21. Dr. Peterson received his medical degree in 1931 from the University of Minnesota.

* * * *

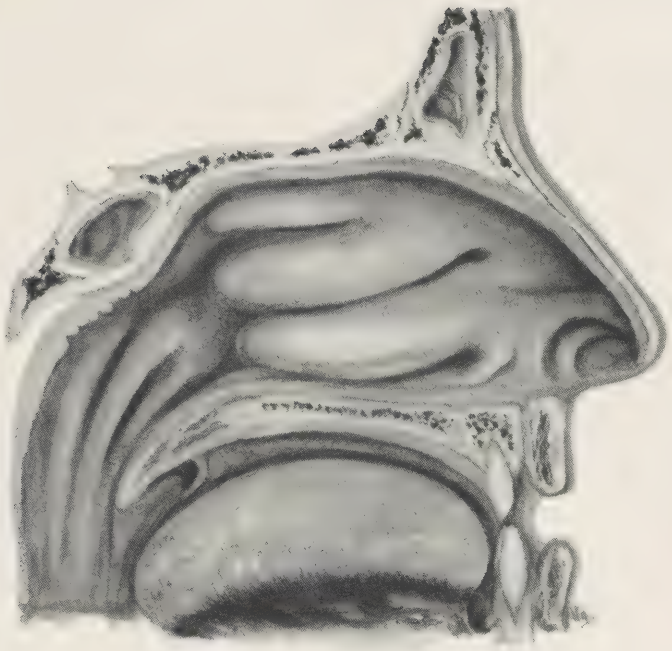
DR. MATTHEW J. LYNCH, 87, died Aug. 8 in Minneapolis. Dr. Lynch graduated from Rush Medical College, Chicago, in 1905. For more than fifty years he was on the staff of St. Mary's Hospital, Minneapolis.

* * * *

DR. JULIUS C. BUSCHER, 74, retired chief of the medical staff of the Veterans Administration Hospital, St. Cloud, died Aug. 8. Dr. Buscher graduated in 1919 from the Christian-Albrechts-Universitat Medizinische Fakultat, Kiel, Germany. He was a member of the Association of American Physicians and Surgeons, and of the University Psychiatric Society.

* * * *

DR. WILLIAM R. BAGLEY, 95, pioneer Duluth physician, died July 28 in Duluth. Dr. Bagley received his medical degree from the University of Michigan in 1898. He was a member of the American College of Surgeons.



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'Sudafed'® brand Pseudoephedrine Hydrochloride .....30 mg.
Bottles of 1 pint.

Dosage and Administration	**Tablets**	**Syrup**
Adults and children over 6 years of age	1	2 tsp.
Children 4 months to 6 years of age	½	1 tsp.
Infants up to 4 months of age	—	½ tsp.

Dosage indicated may be given 3 times daily.

Side effects: While the great majority of patients will experience no side effects on 'Actifed' therapy, those sensitive to the component drugs may exhibit mild stimulation or mild sedation. No serious side effects have been noted.

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NOVEMBER 1965

INDEX MEDICUS



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Papaverine hydrochloride	16 mg.
Aluminum aspirin	300 mg.
Phenylephrine hydrochloride	5 mg.
Chlorpheniramine maleate	2 mg.
Vitamin C	100 mg.

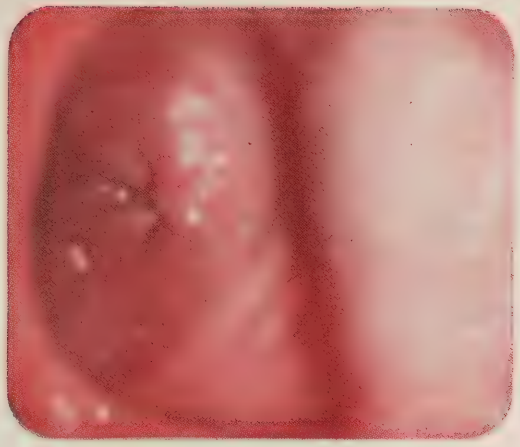
Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

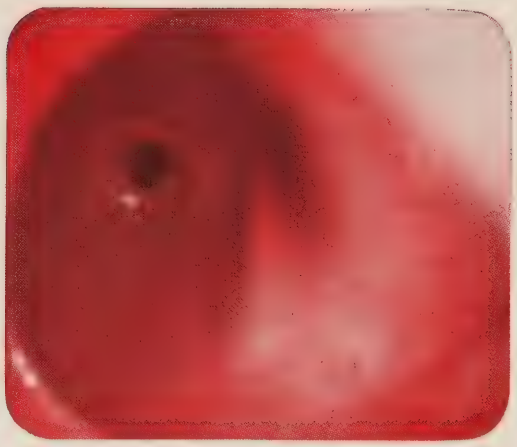
Indications: Cough, congestion, headache, discomfort and muscular aches and pains in coryza, rhinitis, sinusitis, pharyngitis, laryngitis, tracheitis, bronchitis, grippe, influenza and pneumonia.

Side effects and precautions: Side effects are infrequently encountered. Codeine and aluminum aspirin should not be given to patients with known idiosyncrasies to these drugs. Antihistaminic agents may cause drowsiness in susceptible individuals. Colrex Compound should be used with caution in hypertensive patients.

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A/ E. B., male, age 48. Normal antral contraction. Pyloric opening is not seen. It is difficult to differentiate a deep prepyloric contraction from a "pyloric fleurette" or true pylorus.

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Side Effects and Contraindications—Urinary hesitancy, xerostomia, mydriasis and, theoretically, a curare-like action may occur. The drug is contraindicated in patients with glaucoma or severe cardiac disease.

1. Barowsky, H.; Greene, L., and Bennett, R.: Investigators' Clinical Report. Photographs courtesy of Drs. H. Barowsky, L. Greene and R. Bennett.

2. Barowsky, H.; Greene, L., and Paulo, D.: Paper read at Meeting of American Society for Gastrointestinal Endoscopy, Montreal, Canada, May 25-27, 1965.

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. . . but if your patient can't get away, relieve sneezing, running nose, and congestion of colds and sinusitis all day or all night with one

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The Journal-Lancet Volume 85, No. 11, NOVEMBER 1965

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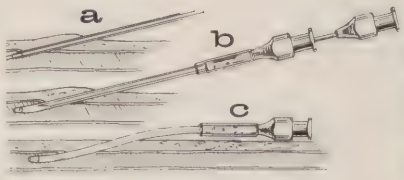
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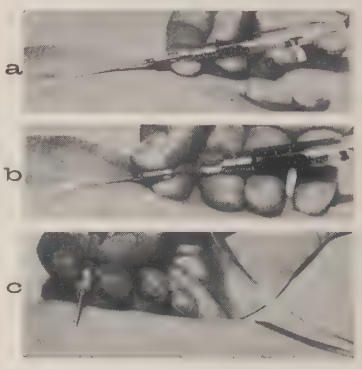
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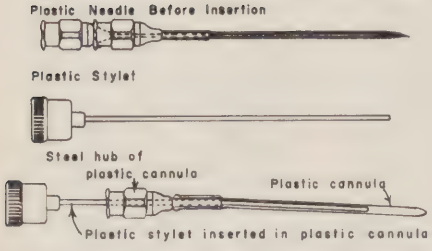




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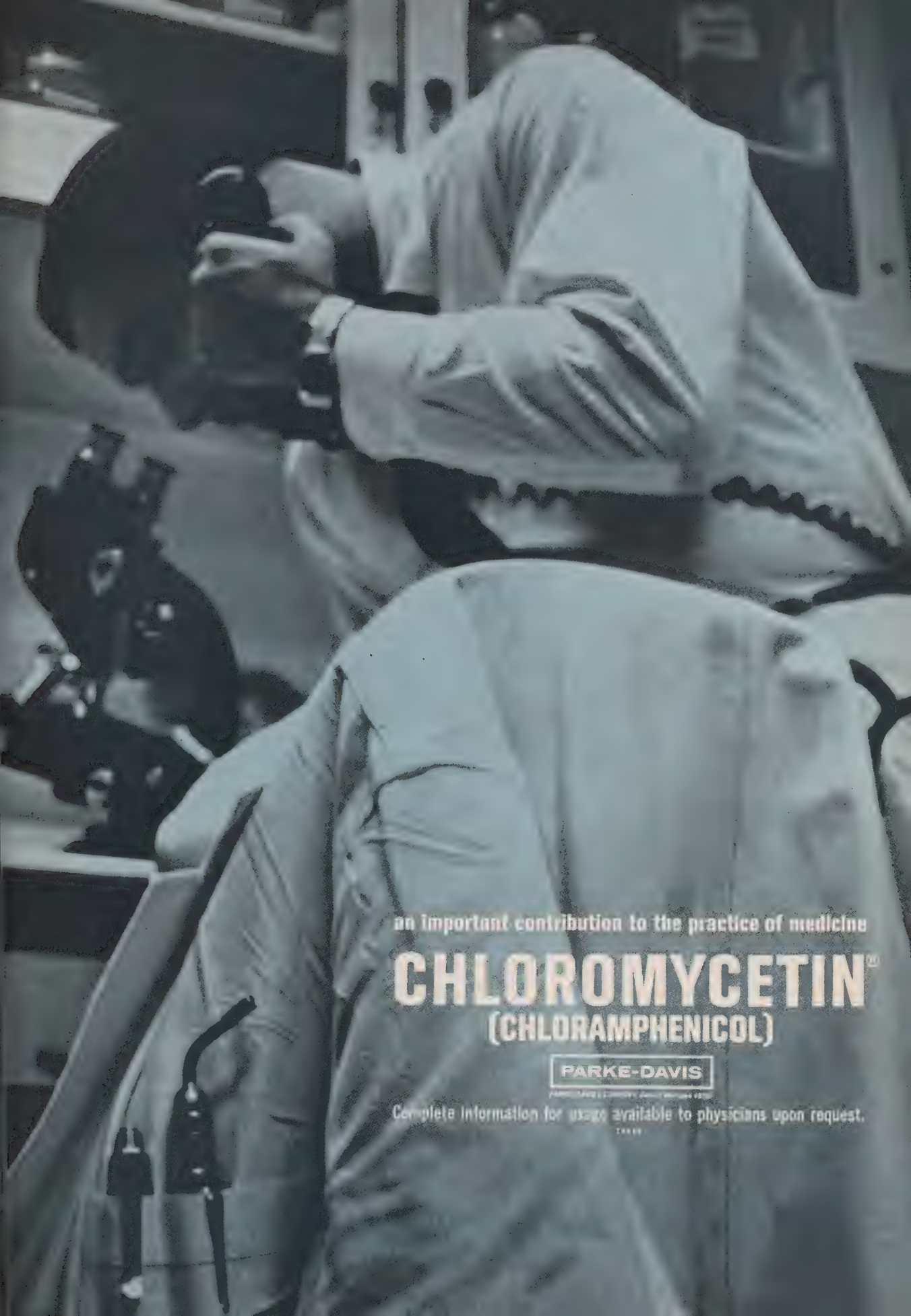
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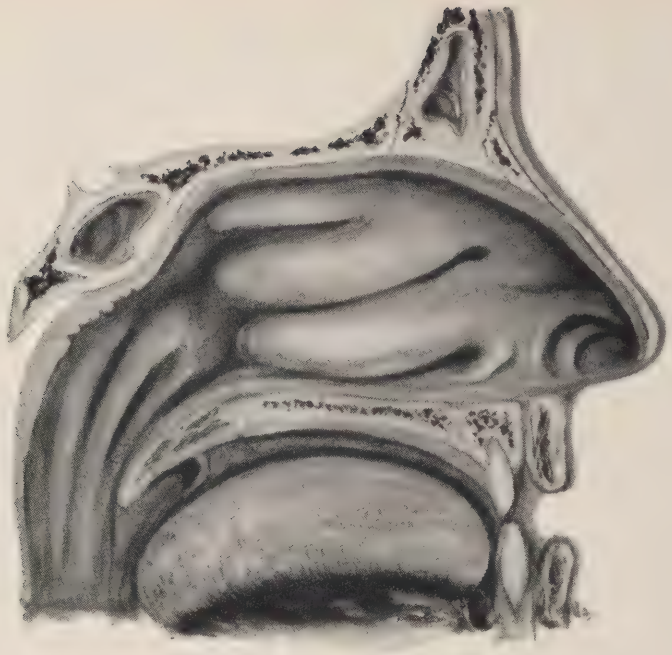
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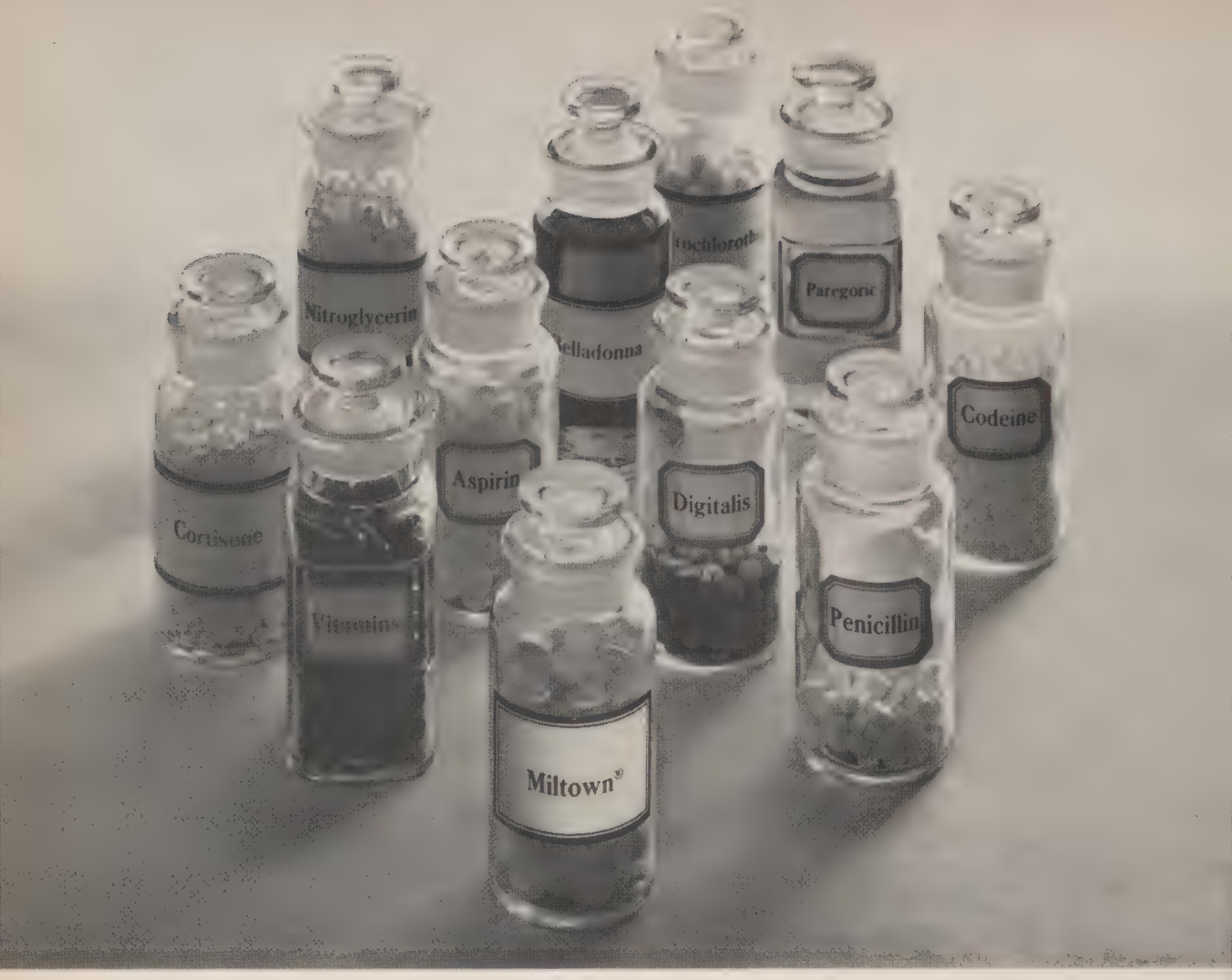
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Sixty-seven years ago this month, Dr. S. Marx White, professor of medicine emeritus of the University of Minnesota, arrived in Minneapolis to work under Dr. Frank Wesbrook at the university. Dr. White's participation in medicine started in 1887 at Sandwich, Ill., when, as a lad of 14, he was allowed to watch his general practitioner grandfather at work. Ever since, medicine has been his consuming interest. In a bit of autobiography, "The Changing Scene in Medicine 1887-1960," Dr. White shares his reminiscences with readers of the December issue of THE JOURNAL-LANCET.

On the clinical side, Dr. Ralph C. Carpenter of the Department of Otolaryngology, Evangelical Mercy Hospitals, Marshalltown, Iowa, takes up "Inhalant Allergies with Headache as the Only Symptom." In this second of a series of articles on allergy for the practitioner, he outlines a rational approach to diagnosis and treatment of headache caused by inhalant allergies.

The series on cardiovascular disease is continued in December with an article on "Instrumentation in a Catheterization Laboratory," by Dr. William F. Mazzitello, director of the Cardiac Catheterization Laboratory, St. Mary's Hospital, Minneapolis. He tells in a clear, straightforward manner what is involved in the equipment and operation of a cardiac laboratory.

Dr. Henry Swan of the Department of Surgery, University of Colorado School of Medicine in Denver, contributes a paper on "Experimental Hemorrhage," as part of a series of articles dedicated to Dr. James J. Waring.



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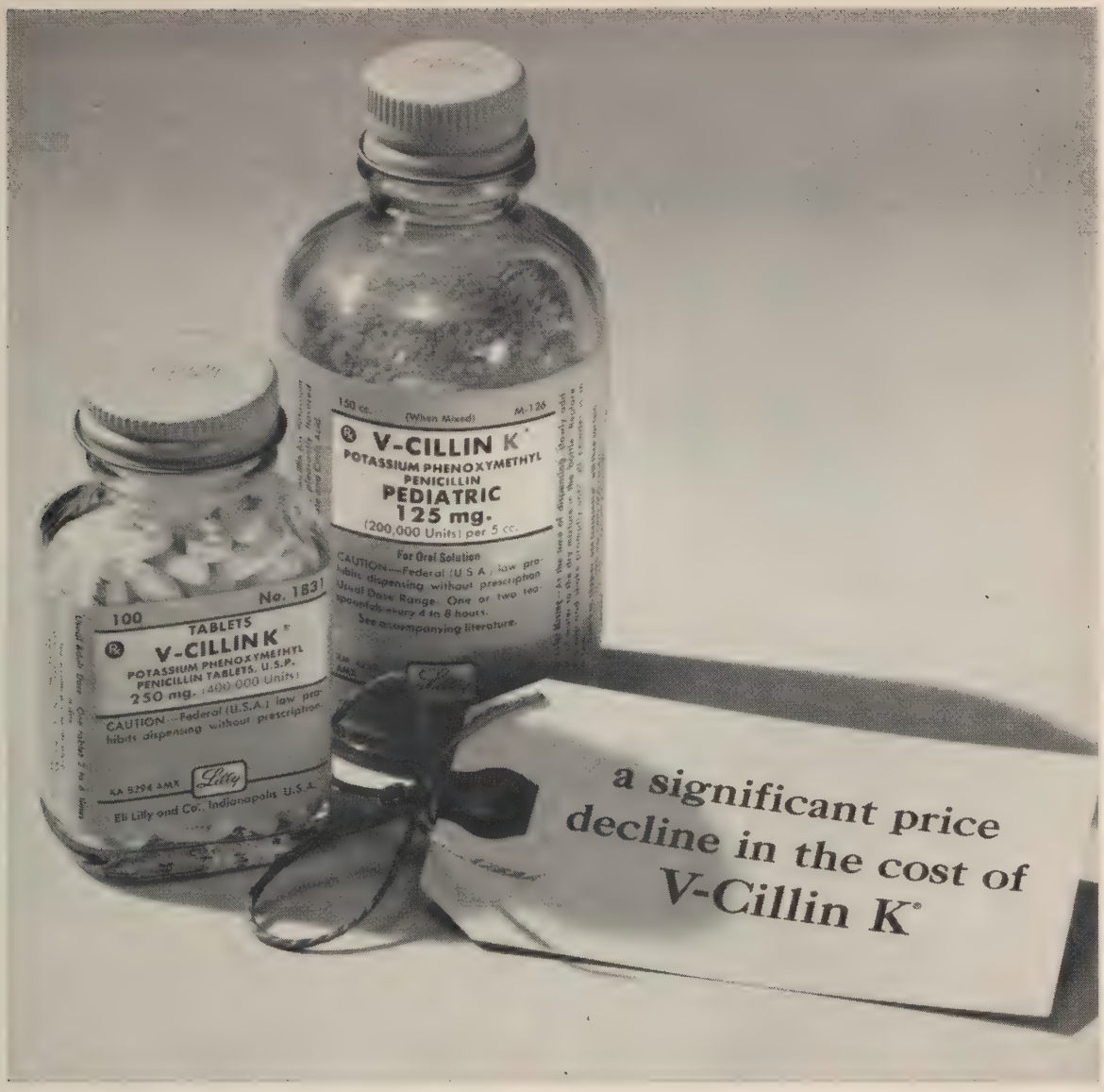
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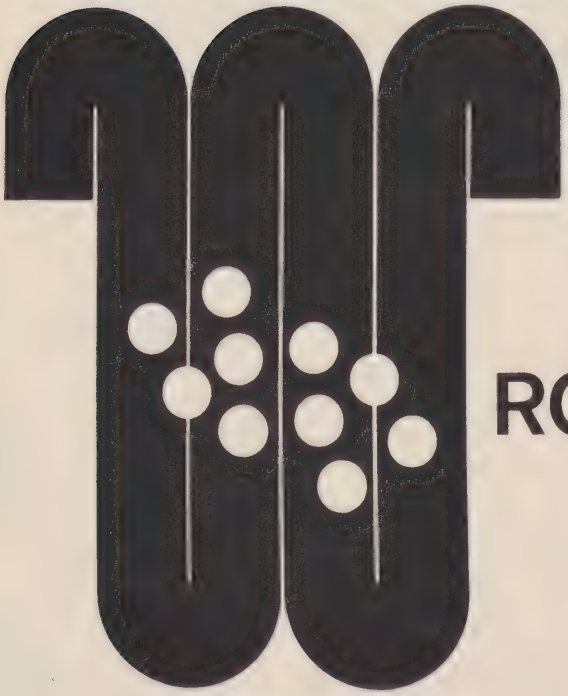
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Special Issue on Pediatrics from the University of Oklahoma

Introduction

HARRIS D. RILEY, JR., M.D.

Oklahoma City

THIS SPECIAL ISSUE from the Children's Memorial Hospital, University of Oklahoma Medical Center, presents a small sample of the diverse and wide-ranging clinical and research activities which typify a children's hospital of today and its activities in child health. The philosophy of the department of pediatrics is that a healthy balance between teaching, patient care, and research, both clinical and basic, should exist in a children's hospital. It is believed that the reader will obtain this flavor after perusal of the presentations in this special issue devoted to pediatrics. Despite the diversity of the topics covered, the concept of developmental biology is a continuing thread throughout the studies in this special issue.

This issue includes contributions, not only from the various sections of the department of pediatrics such as pediatric cardiology, pediatric hematology, pediatric neurology, and the Child Study Center, but also from other departments of the Children's Memorial Hospital—such as the departments of radiology and otorhinolaryngology.

Beargie's paper on anicteric erythroblastosis has documented the situation that all pediatricians have occasionally encountered; namely, the occurrence of erythroblastosis with significant anemia but without hyperbilirubinemia and jaundice. Nida and Bracken, in studying the important relationships between infection and the abnormal secretions in cystic fibrosis of the pancreas, have pointed out how the electron microscope can be utilized in clinical research. Although idiopathic thrombocytopenic purpura is not an uncommon disease in pediatric wards, pediatricians generally are familiar with only the immediate outcome of the individual case, but not the long-term course of children with this disorder. Haddy has detailed this along with the clinical and laboratory findings in twenty-five cases. The establishment of clinical study centers for birth defects by the National Foundation has focused increased interest on congenital malformations, particularly those of the central nervous system. An example of the increased effort being devoted to these disorders is provided in the paper by Jabbour and Vallion. In addition, the possible prognostic value of a long-recognized roentgenographic sign, craniolacunia, is raised. The cardiovascular aspects represent an important clinical component of the various collagen diseases. Thompson has made an important contribution for the physician interested in these disorders by assembling in one place a comprehensive treatment of these manifestations. The relative role of hereditable and environmental factors in another congenital malformation, congenital heart disease, is also discussed. Howard and Riley have reviewed the epidemiologic and

HARRIS D. RILEY, JR., *is professor of Pediatrics and head of the Department, University of Oklahoma School of Medicine; pediatrician-in-chief, Children's Memorial Hospital, Oklahoma City.*

clinical aspects of a rather large number of cases of tetanus and have pointed out the importance of this disease in the newly born. Steger and Worley have outlined the clinical and radiographic features of a little-recognized entity, intramural hematoma of the duodenum.

Two papers from the Child Study Center, a special section of the department of pediatrics devoted to mental retardation and other neurological handicaps in children, point out the increasing role of the pediatrician in handling learning and perceptual disorders.

Recent years have seen tremendous advances in pediatric radiology. None have been more rapid or important than the refinement and productivity of case-finding techniques related to the genitourinary tract of infants and children. Shopfner has brought us up-to-date in this field, pointing out the causative relationship of infection to reflux and the value of the voiding cystogram as a diagnostic measure.

Every pediatrician has been confronted with the infant with noisy respiration. Snow's paper, in addition to reviewing the pathogenesis and clinical manifestations, outlines a practical and orderly diagnostic approach to such patients.

In addition to the individual authors of the presentations included in this issue, I also wish to acknowledge the efforts of the house staff, technicians, and secretaries of the Children's Memorial Hospital, without whose efforts many of these studies and reports would not be possible. In particular, I am indebted to Dr. Ben H. Nicholson, clinical professor of pediatrics, for his invaluable editorial assistance in assembling this special issue.

Idiopathic Thrombocytopenic Purpura in Children: An Analysis of 25 Cases

THERESA B. HADDY, M.D.
Oklahoma City

IDIOPATHIC THROMBOCYTOPENIC purpura (ITP, primary thrombocytopenic purpura, essential thrombocytopenic purpura, purpura hemorrhagica, or Werlhof's disease) is a disorder of unknown etiology characterized by decreased circulating platelets with resultant petechiae, ecchymoses, and sometimes hemorrhage. This paper presents a critical evaluation of 25 cases seen recently at the Children's Memorial Hospital of the University of Oklahoma Medical Center. Special attention is given to the incidence of associated anomalies.

MATERIAL AND METHODS

The charts of all patients discharged from Children's Memorial Hospital with the diagnosis of idiopathic thrombocytopenic purpura during the years 1954 through 1964 were reviewed. The children were referred from both urban and rural portions of the state of Oklahoma. All were under 15 years of age. Although a variety of socioeconomic backgrounds were represented, the majority were from indigent families. The patients were studied on general pediatric wards but each child was seen by a pediatric hematology consultant who concurred in the diagnosis.

The chief criterion for the diagnosis was a platelet count of 60,000 per cubic millimeter or less. Other criteria were the absence of known previous exposure to drugs or toxins, concomitant infection or infestation, anemia other than that due to acute or chronic blood loss, and leukopenia or leukocytosis. The diagnosis of idiopathic thrombocytopenic purpura is one of exclusion. No case was considered acceptable, therefore, unless there was evidence in the medical record that the following diseases had been ruled out: leukemia, aplastic anemia, lupus erythematosus, the reticuloendothelioses, lipid and other storage diseases, portal hypertension, thrombotic thrombocytopenic purpura, Aldrich's syndrome (eczema, thrombocytopenia, and anemia), hemolyticuremic syndrome, and thrombocytopenia associated with hemangioma. Since congenital thrombocytopenic purpura is frequently due to an immune mechanism, patients with this disorder were eliminated from the study.

When the above criteria were applied, only 3 cases were discarded. One was a two-month-old white girl who had an acute episode of thrombocytopenia that occurred during a mild bout of rhinitis and diarrhea. The thrombocytopenia relented as the respiratory and gastrointestinal symptoms subsided. Her thrombocytopenia was therefore thought to be secondary to a viral infection. Another was a 3-year-old white boy with a four-week history of spontaneous ecchymoses, petechiae, and bleeding gums. At the time of admission he had purpura and a platelet count of 122,500 per cubic millimeter, but all of the other clotting studies were normal. During his hospital stay the platelet count rose to 243,000 per cubic millimeter and his purpura faded. Bruising and bleeding did not recur. His course may have represented a spontaneous remission of idiopathic thrombocytopenic purpura. The third child was an 8-year-old Indian girl who initially seemed to have fairly typical idiopathic thrombocytopenic purpura. The number of megakaryocytes in her bone marrow, however, was decreased. She subsequently developed neutropenia and, still later, anemia. When the anemia appeared, ten months after the first signs of illness, the diagnosis of idiopathic pancytopenia became evident.

Twenty-five cases were considered acceptable according to the stated criteria and were included in the study. A patient whose symptoms were present for less than six months was arbitrarily classified as having an acute case, and one whose symptoms persisted for longer than six months, a chronic course. On this basis, 9 children had acute and 16 had chronic idiopathic thrombocytopenic purpura.

THERESA B. HADDY *is from the Department of Pediatrics and the Children's Memorial Hospital, University of Oklahoma Medical Center.*

TABLE 1

INITIAL CLINICAL FINDINGS OF 25 CHILDREN WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA

Patient	*Race, sex, age (yrs.)*	*Preceding infections*	*Symptoms*	*Duration of symptoms*	*Purpura*	*Spleen palpable*	*Platelet count (per cu. mm.)*	*Hemoglobin (gm.%)*	*Megakaryocytes in bone marrow*
1	W M 6 9/12	No	Easy bruising, epistaxis, hematuria	4 yrs.	+	+	3,000	7.5	Adequate
2	W F 6 11/12	No	Easy bruising, epistaxis	6 yrs., 11 mos.	0	0	21,000	13.0	Decreased
3	W M 14 4/12	No	Easy bruising, epistaxis, hematoma	3 wks.	+	+	8,000	10.8	Decreased
4	I M 10 9/12	No	Easy bruising, epistaxis	6 yrs.	+	0	9,000	13.0	Increased
5	W F 9 8/12	No	Easy bruising, bleeding from gums	3 days	+	0	7,000	12.5	Increased
6	W F 9	No	Easy bruising, bleeding from oral membranes	8 mos.	+	0	34,000	11.2	Increased
7	W F 4 9/12	Tonsillitis	Easy bruising, epistaxis	6 days	+	+	7,000	8.7	Increased
8	W M 7 8/12	No	Easy bruising	3 mos.	+	0	0	11.7	Adequate
9	W F 11 3/12	No	Epistaxis, vaginal bleeding	8 mos.	0	0	13,000	12.0	Adequate
10	W M 7 6/12	No	Easy bruising	3 yrs.	+	+	45,000	13.5	Adequate
11	W M 3 10/12	Rubella	Easy bruising, epistaxis	6 days	+	0	47,000	11.6	Decreased
12	W M 8 6/12	No	Epistaxis, bleeding from gums, melena	5 days	+	+	7,000	8.5	Increased
13	W F 3	Undetermined febrile illness	Easy bruising, epistaxis	5 days	+	+	57,000	12.0	Adequate
14	W F 3 5/12	No	Easy bruising	1 yr.	+	0	44,000	10.9	Increased
15	W M 8 1/12	No	Easy bruising, epistaxis, hematemesis	6 yrs.	+	0	25,000	11.0	Adequate
16	W F 11 10/12	No	Easy bruising	9 mos.	+	0	20,000	12.9	Increased
17	W F 3	No	Easy bruising, epistaxis, hematemesis, melena	8 mos.	+	0	15,000	8.9	Increased
18	W F 3 3/12	No	Easy bruising	1 yr.	+	0	60,000	12.4	Increased
19	I M 4 2/12	No	Easy bruising	3 yrs.	+	0	30,000	11.7	Adequate

TABLE 1 (continued)

Patient	Race, sex, age (yrs.)	Preceding infections	Symptoms	Duration of symptoms	Purpura	Spleen palpable	Platelet count (per cu. mm.)	Hemoglobin (gm.%)	Megakaryocytes in bone marrow
20	I M 6 6/12	Mumps and tonsillitis	Easy bruising, epistaxis	2 mos.	+	0	10,000	14.6	Adequate
21	W M 7 3/12	No	Easy bruising, epistaxis	3 yrs.	+	0	6,000	12.4	Increased
22	W M 4 7/12	No	Easy bruising, epistaxis, hematemesis	1 yr., 6 mos.	+	0	55,000	6.4	Adequate
23	W F 7 4/12	Tonsillitis	Easy bruising, bleeding from gums	5 wks.	0	0	44,000	12.3	Adequate
24	W M 13	No	Easy bruising, hematuria	6 mos.	+	0	30,000	13.4	Adequate
25	W F 10 3/12	No	Easy bruising, epistaxis, bleeding from gums	2 yrs.	+	0	23,000	14.6	Adequate

CLINICAL FINDINGS

The 25 children ranged in age from 3 to 14 years (Table 1). Thirteen were boys and 12 were girls. Twenty-two of the children were Caucasians and 3 were American Indians.

When the children were first seen, their symptoms had persisted for periods ranging from five days to nearly seven years. Five (20%) of the 25 children had febrile illnesses preceding the onset of hemorrhagic manifestations by one to three weeks. Three had tonsillitis and 1 each had mumps (along with tonsillitis), rubella, and a febrile episode of undetermined nature. One child (No. 8) had a tick bite three weeks before the onset of his illness but, since he did not become febrile at any time, the bite was apparently not related to his thrombocytopenia.

The most common sign by far, as expected, was easy bruising[1,2] and the next most common sign was epistaxis (Table 2). Other signs were bleeding from the gums or oral mucous membranes, hematemesis, melena, hematuria, hematoma, and vaginal bleeding. Hematemesis and melena were probably due to swallowed blood from the nasal or oral membranes rather than from hemorrhage originating in the gastrointestinal tract. Patient No. 9, an 11-year-old girl, had an unusual history for a pediatric patient. The first sign of her disease was hemorrhage associated with spontaneous abortion of a two months' pregnancy. She subsequently had excessive vaginal bleeding and epistaxis with each menstrual period until her spleen was removed.

The most common physical finding, again as expected, was purpura.[1,2] This manifestation was observed in all except 3 of the children at the time of initial examination. The physical findings were not always consistent with the history. Two of the patients (No. 2 and 23) were said to have purpura but actually did not. Conversely, petechiae were present on 1 patient (No. 12) in whom a history of purpura was denied. None of the 25 children appeared ill although those who had anemia were pale and listless. An unexpected finding was that 6 (24%) of the 25 patients had palpable spleens as noted by 1 or more observers. None, however, was markedly enlarged.

Five (20%) of the 25 patients (No. 1, 2, 16, 18, and 24) are especially noteworthy because of interesting associated anomalies. The abnormalities followed no discernible pattern in regard to number. One child (No. 2) had many anomalies, another (No. 16) had 2, and the other 3 had 1 each. Likewise, there was diverse system involvement. Cardiovascular and genitourinary anomalies occurred in each of 2 patients but central ner-

TABLE 2

SUMMARY OF PRESENTING SYMPTOMS OF 25 CHILDREN WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA

Easy bruising	23
Epistaxis	15
Bleeding from gums or oral mucous membranes	5
Hematemesis	3
Melena	2
Hematuria	2
Hematoma	1
Vaginal bleeding	1
Hemarthrosis	0
Central nervous system bleeding	0

vous system, gastrointestinal, bone and joint, eye, ear, and reticuloendothelial anomalies appeared in only 1 patient each. Patient No. 1 had a cleft palate that had been previously repaired. Multiple congenital anomalies including mental retardation, deformed ears, congenital dislocation of the left hip, left talipes calcaneovalgus, agenesis of both thumbs, absence of the right kidney, and a patent ductus arteriosus were present in patient No. 2. The patent ductus was ligated without difficulty subsequent to splenectomy. Patient No. 16 had a duplication of the esophagus that had been previously noted as a mediastinal mass. It was excised at the time of splenectomy. She later had an operation for bladder neck obstruction. Patient No. 18 had esotropia of the right eye. This was corrected by a surgical procedure after splenectomy. Patient No. 24 was discovered to have many lipid-containing macrophages in his spleen upon microscopic examination. Although this finding was suggestive of lipid storage disease, the patient was an intelligent 13-year-old boy who had no physical abnormalities except for mild obesity and Cushingoid appearance secondary to corticosteroid therapy. He had a good platelet response after splenectomy and his platelet count was normal three months later. His clinical condition and course clearly did not fit the picture of lipid storage disease. This unusual finding has recently been described.[3,4]

All of the 25 patients had thrombocytopenia with platelet counts ranging between 0 and 60,000 per cubic millimeter. Peripheral smears in each case confirmed that platelets were decreased in number. Anemia, as represented by hemoglobin values below 10.0 gm. percent, was present in 5 (20%) of the children. In all patients the anemia was secondary to bleeding. Two of the anemic patients (No. 1 and 17) had hypochromic red cells and histories consistent with chronic blood loss. Two others (No. 7 and 12) had normochromic red cells and histories consistent with acute blood loss. The remaining patient (No. 22) had mildly hypochromic red cells with a disproportionately low hemoglobin of 6.4 gm. percent. His history included both recurrent mild bleeding and recent marked hemorrhage. Each of the patients who was seen after 1958 (No. 13 through 25) had several studies for either lupus erythematosus (L.E.) cells or L.E. antinuclear antibodies in order to rule out lupus erythematosus.[5] All such investigations were negative. Eosinophilia was not a prominent feature in this group of patients. Only 1 child (No. 4) had eosinophilia of the peripheral blood, with 11% eosinophils, and none of the children had

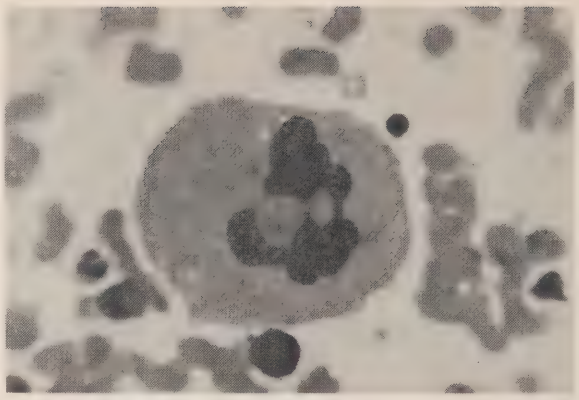


Fig. 1. Megakaryocyte from bone marrow of patient with idiopathic thrombocytopenic purpura. No platelets are being produced. Wright, × 97

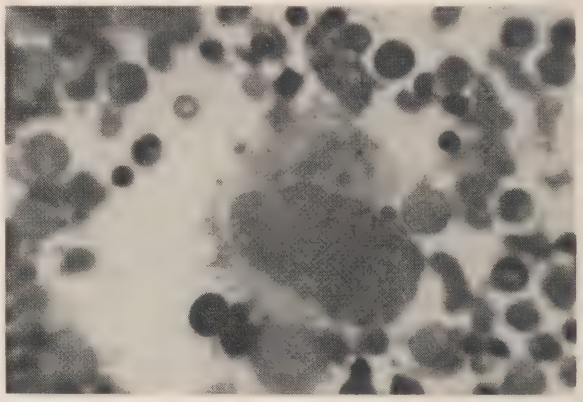


Fig. 2. Mature megakaryocyte from normal bone marrow. Platelet production is apparent. Wright, × 97

eosinophilia of the bone marrow. One (4%) of 25 patients represented a smaller than usual percentage for Children's Memorial Hospital. Of all patients seen during 1963, an average of 8.8% had 10% or more eosinophils in their peripheral blood.[6] Bone marrow examinations were carried out on all of the patients. Megakaryocytes were decreased in number in 3 of the 25 children and adequate or increased in the other 22. Whether megakaryocytes were decreased, adequate, or increased in number, platelet production in every instance appeared markedly reduced (Fig. 1) as compared to normal (Fig. 2).

THERAPY AND RESULTS

Twenty-four of the 25 children with idiopathic thrombocytopenic purpura received specific therapy consisting of one or more of the following: corticosteroids, adrenocorticotropin, fresh frozen plasma, and splenectomy (Table 3). A number of the 24 children also required treatment with supportive measures. The remaining child (No. 11) was given neither specific nor supportive therapy.

TABLE 3

THERAPY GIVEN 25 CHILDREN WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA*

Patient	*Course†*	*Adrenal corticosteroids*	*Adrenocorticotropic hormone*	*Fresh frozen plasma*	*Splenectomy*	*Recovery*
1	Chronic	0	0	0	+	Yes
2	Chronic	0	0	0	+	No
3	Acute	+	+	0	0	Unknown
4	Chronic	0	0	0	+	Yes
5	Acute	0	+	0	0	Yes
6	Chronic	+	++	0	+	Yes
7	Acute	+	+	0	0	Yes
8	Acute	+	0	0	+	Yes
9	Chronic	0	0	0	+	Yes
10	Chronic	+	0	0	+	Yes
11	Acute	0	0	0	0	Yes
12	Acute	+	0	0	0	Yes
13	Acute	+	0	0	0	Yes
14	Chronic	++	+	0	+	Partial
15	Chronic	++++	++	+	+	No
16	Chronic	++	0	+	+	Yes
17	Chronic	+	+	+	+	Yes
18	Chronic	++	++	+	+	Yes
19	Chronic	+	0	0	0	Yes
20	Acute	+	+	0	0	Yes
21	Chronic	+	++	0	+	Yes
22	Chronic	+	0	0	0	Yes
23	Acute	+	0	0	0	Yes
24	Chronic	+	+	0	+	Yes
25	Chronic	+	+	0	+	Yes

*Pluses indicate number of courses of therapy heading the column.

†The patient's course was considered acute if symptoms were present for less than 6 months, chronic if longer than 6 months.

Patients who achieved platelet counts of 200,000 per cubic millimeter or more were considered to have complete responses, those who achieved platelet counts between 100,000 and 200,000 per cubic millimeter were considered to have partial responses, and those whose platelet counts remained below 100,000 per cubic millimeter were considered to have no response. On this basis, 21 of the 25 patients had complete responses, 1 (No. 14) had a partial response, and 2 (No. 2 and 15) had no response. The final course of 1 (No. 3) is unknown. Twenty-two (91.7%) of the 24 children who could be followed achieved full or partial remissions.

Corticosteroids. This form of therapy was used in 19 of the 25 children. Prednisone, the glucocorticosteroid used in all cases, was administered in dosages that approximated 2.2 mg. per kilogram per day, with a minimum starting dose of 20 mg. per day and a maximum of 60 mg. per day. Most courses of therapy lasted approximately three or four weeks. When more than one course of prednisone therapy was administered, the drug was tapered and stopped for an interval between courses. Five of the 19 children who were treated with prednisone had complete responses and 14 did not. Of the children who reacted, 3 (No. 12, 13, and 23) had acute and 2 (No. 19 and 22) chronic idiopathic thrombocytopenic purpura. None of the 5 required further treatment. The dosage regimen used is recommended by a number of investigators[5,7] but others feel that smaller doses of 1.0 mg. per kilogram per day are more effective.[8] There is evidence that long-term large doses of prednisone can cause thrombocytopenia.[9] Since the patients in this study received neither massive nor prolonged doses, prednisone-induced thrombocytopenia is improbable. The dosage used, however, may not have been the optimum prednisone dosage for idiopathic thrombocytopenic purpura.

Adrenocorticotropin (ACTH). Twelve of the 25 children were treated with ACTH. Intravenous daily doses of 25 to 40 units were administered in 5% glucose in distilled water over eight to eighteen hours for courses of therapy varying from three to ten days. Seven reacted to ACTH and 5 did not. One child (No. 5), who had acute idiopathic thrombocytopenic purpura, had received no previous treatment; she had a good platelet response and required no further therapy. Six of the patients who reacted to ACTH had previously failed to achieve platelet elevations with prednisone. Two of the 6 (No. 7 and 20) achieved full remissions of their disease after ACTH and needed no subsequent therapy. The other 4 (No. 18, 21, 24, and 25) had complete or partial platelet responses to ACTH but failed to maintain the responses and eventually had their spleens removed.

Four patients, all with chronic idiopathic thrombocytopenic purpura, received 2 units each of fresh frozen plasma.[10] No responses were obtained.

Splenectomy. Fifteen of the 25 children had splenectomy (Table 4). Thirteen achieved remissions and 2 did not. The criterion for this form of therapy was chronicity or persistence of symptoms for six months or longer. All 15 patients, with a single exception (No. 8), fulfilled this criterion. The recovery rate of 12 (85.7%) of 14 patients with chronic idiopathic thrombocytopenic purpura is comparable to the expected rate of 80 to 85%.[11,12] The reason why patient

TABLE 4

RESULTS OF SPLENECTOMY IN 15 CHILDREN WITH IDIOPATHIC THROMBOCYTOPENIC PURPURA

Patient	*Weight of spleen (gm.)*	*Size of spleen (cm.)*	*Morphology of spleen*	*Maximum postsplenectomy platelet response (per cu. mm.)*	*Maximum postoperative platelet response (day)*
1	—	8.0 × 6.0 × 4.0	Reticular hyperplasia	538,000	2
2	28	8.0 × 2.5 × 0.3	Reticular proliferation	36,000	7
4	95	—	Reticular hyperplasia	269,000	10
6	70	9.5 × 5.3 × 2.8	Congestion of spleen	820,000	11
8	55	11.0 × 6.0 × 4.0	Congestion of spleen	994,000	8
9	160	10.0 × 16.0 × 6.0	Congestion of spleen and extramedullary hematopoiesis	353,000	9
10	95	—	Extramedullary hematopoiesis	257,000	2
14	60	9.0 × 6.5 × 2.0	Congestion of spleen	2,474,000	6
15	60	—	Myeloid metaplasia	130,000	5
16	130	10.0 × 7.0	Congestion of spleen	771,000	8
17	—	7.0 × 5.0 × 2.0	Congestion of spleen	1,602,000	7
18	70	—	Congestion of spleen	1,266,000	5
21	130	12.0 × 8.5	Normal spleen	1,000,000	13
24	210	10.0 × 8.0 × 10.0	Many abnormal lipid-containing macrophages	1,210,000	13
25	72	—	Normal spleen	1,800,000	6

No. 8 had a splenectomy after only three months of symptoms is not clear. Although he recovered after splenectomy, he might well have had a spontaneous remission if surgery had been deferred. Eleven of the 15 children who had splenectomy had been previously treated with corticosteroids; none had reacted. Eight of the 15 children had been previously treated with ACTH; 4 had reacted but had not maintained their platelet responses. All of the spleens were normal or slightly enlarged in size. Three patients had small abdominal accessory spleens that were identified and removed at the time of operation. Patient No. 1 had 3 and patients No. 6 and 17 had 1 each. All of the spleens, with 1 exception, had normal microscopic morphology, splenic congestion, reticular hyperplasia, extramedullary hematopoiesis, or myeloid metaplasia when studied in the usual routine manner by a pathologist. The exception was the spleen of patient No. 24 who has been discussed under clinical findings. His spleen contained large numbers of lipid-containing macrophages (Fig. 3). Maximum platelet counts after splenectomy, except in 2 patients who failed to react, were 257,000 to 2,474,000 after two to thirteen days. None of the patients were treated with anticoagulants. None are known to have had serious postsplenectomy infections.[7] Of the 2 children who failed to react to splenectomy, 1 (No. 2) was a 6½-year-old girl who had easy bruising and epistaxis since birth, reduced numbers of megakaryocytes in her marrow, and multiple congenital anomalies. The other patient (No. 15), who was an 8-year-old white boy, had a history of easy bruising and epistaxis for six years, adequate numbers of megakaryocytes in his bone marrow, and no other apparent physical abnormalities. All therapy has been unsuccessful and he continues to have chronic thrombocytopenia. He is now 12 years old and has had a number of hospital admissions subsequent to splenectomy for bleeding into the penis, epistaxis severe enough to require blood transfusion, and hemarthrosis of the right hip. A meticulous search for other underlying disease has been fruitless. Radioisotope studies for an accessory spleen were nonproductive. Exploratory laparotomy is under consideration. A disappointingly small number of the other patients have been available for postsplenectomy

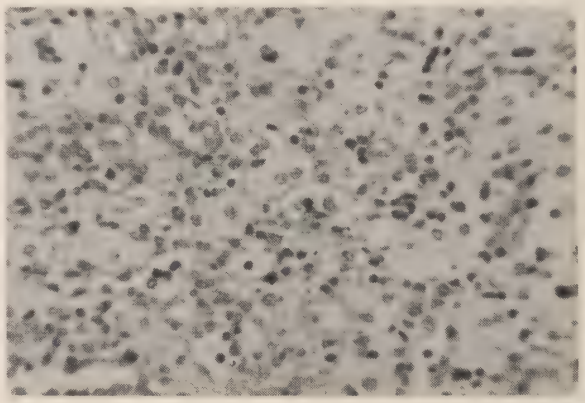


Fig. 3. Abnormal lipid-containing macrophages in spleen of patient No. 24. Hemotoxylin and eosin, × 43

study. In the absence of satisfactory follow-up, it is not possible to presume with certainty that patients have remained in remission nor can subtle underlying disease be absolutely excluded.

COMMENT

Two observations resulting from this study, the response rate to ACTH and the high incidence of associated anomalies, deserve brief emphasis.

The use of ACTH in thrombocytopenic states is well known but the drug is not widely employed, probably because of practical difficulties. In this series, 7 of 12 children so treated reacted with platelet increases. The observation that 6 of the 7 had previously failed to improve on prednisone must be interpreted cautiously. In most cases ACTH was the second agent used. A second course of prednisone might have been successful even though the first was not. Both drugs were tested against small numbers of patients. Neither treatment group was compared to a similar control group in order to determine the incidence of spontaneous remissions. The 5 patients who responded to prednisone maintained normal platelet levels and needed no other therapy. Four of the 7 patients who responded to ACTH, on the other hand, failed to maintain platelet elevations and later underwent splenectomy. Although ACTH appears in this study to be more effective than corticosteroids, the observation might be invalid. It may be concluded, however, that ACTH therapy deserves further study in idiopathic thrombocytopenic purpura because its beneficial effect may justify the inconvenience of intravenous administration.

That 5 (20%) of the 25 children had one or more associated congenital anomalies is worthy of note. The child (No. 2) with decreased megakaryocytes and multiple congenital anomalies including skeletal and cardiac defects may have had congenital hypoplastic thrombocytopenia (primary amegakaryocytic thrombocytopenia).[13,14] If she were deleted from the study, however, 4 of 24 children (16.6%) would still seem to be a surprisingly high percentage. The appearance of concomitant anomalies with idiopathic thrombocytopenic purpura has not been pointed out previously. There is no obvious explanation for this association. It is suggested that observation of other groups of patients with this disease may confirm the observation.

SUMMARY

Symptoms, findings, and management of 25 patients with idiopathic thrombocytopenic purpura admitted to a referral center children's hospital are reviewed. Of 19 who received prednisone, 5 had platelet responses; of 12 who received adrenocorticotropin, 7 had platelet elevations although 6 of the 7 had previously failed to respond to prednisone; of 15 who had splenectomy, 13 had platelet responses; and of 24 who could be followed, 22 (91.7%) achieved remissions from their disease. Five (20%) of the 25 children had one or more associated anomalies.

I wish to thank Dr. Robert M. Bird for critically reviewing the manuscript, Dr. John C. Kramer and Dr. John M. Hill for supplying the medical record of patient No. 25, and Mrs. Anita Tucker and Mrs. Barbara Wilson for furnishing technical assistance.

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Tetanus: Epidemiologic and Clinical Aspects of 72 Cases

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TETANUS HAS COME to be regarded as a rare disease in most sections of this country. Recent studies have documented the declining incidence of reported tetanus in this century and have identified only some states of the deep South as having excessive morbidity and mortality from tetanus at this time.[1,2] In the past ten years, despite widespread immunization with tetanus toxoid, there has been very little change in the nation-wide incidence of tetanus. This has remained in the range of 300 to 400 cases each year. Recent reports have identified certain "high-risk" groups including Negro and Latin American newborns, narcotic addicts, and individuals with heavy occupational exposure to soil and animals.

The occurrence of several cases of tetanus from the Infectious Disease Service of Children's Memorial Hospital during 1963 prompted a review of our experience and of the recent literature on this subject. It was found that our experience has been fairly extensive and representative of the usual type of tetanus seen today.

METHODS AND DEFINITIONS

The medical record of every patient with a final diagnosis of tetanus seen at either the Children's Memorial Hospital or University Hospital, University of Oklahoma Medical Center, during the period 1946 through 1963 was reviewed. Cases were divided by age groups into neonatal (up to 28 days of age), childhood (29 days to 14 years), and adolescent and adult (over 14 years). The severity of the case on admission was classified as mild (local spasm and trismus or both), moderate (opisthotonus), severe (generalized spasms and convulsions), and fulminant (all of the above plus rapid progression to death within twenty-four hours of admission). The first symptom or sign noted was recorded; if 2 or more occurred simultaneously all were recorded. The immunization status was classified as follows: (1) none—no injection of tetanus toxoid had been received, (2) inadequate—partial or complete primary series but no booster at the time of injury, (3) complete—primary series plus booster at time of injury, and (4) unknown. Incubation period was judged to be the period from the time of injury until the onset of symptoms, although it was apparent in some cases that contamination of the wound could have occurred for several days following injury. Cases were classified as rural or urban by their location at the time of injury.

RESULTS

Incidence of tetanus. A total of 72 cases of tetanus occurred during the study period. There were 13 cases occurring in the neonatal period, 35 in infants and children from 29 days to 15 years of age, and 24 in patients over 15 years of age. As shown in table 1, 49 of the total 72 cases occurred in infants and children. The 2 peak periods of incidence were the neonatal period and from 2 to 3 years of age when there were 13 and 12 cases, respectively. Only 3 cases occurred in adolescents and only 1 in the age group 21 through 30 years. The distribution of cases among adults over the age of 30 and the fatalities among the various age groups are shown in table 1. Figure 1 demonstrates the cases and fatalities by year of occurrence in 3 age categories—neonatal, infants and children, and adolescents and adults. Thirteen cases of neonatal tetanus with 9 deaths (case-fatality rate of 69%) were seen; no improvement in the incidence or mortality of neonatal tetanus was observed during this period. For infants and children over the age of 29 days, there were 35 cases with 8 deaths. During this period the incidence of tetanus in

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TABLE 1

DISTRIBUTION OF CASES AND FATALITIES BY AGE

	Number cases	*Number deaths*
0-28 days	13	9
29 days-1 year	1	
1 year	1	
2-3 years	12	4
4-5 years	6	2
6-7 years	5	
8-9 years	4	
10-11 years	2	
11-12 years	1	
12-13 years	1	
13-14 years	2	2
15-20 years	3	
21-30 years	1	
31-40 years	4	2
41-50 years	6	3
51-60 years	5	1
61-70 years	3	2
71-80 years	2	2
TOTAL	72	27

TABLE 2

SEX, RACE, AND RURAL-URBAN DISTRIBUTION OF CASES OF TETANUS

	Neonatal	*Infants and children*	*Adolescents and adults*
Male	11	19	19
Female	2	13	8
White	5	24	23
Negro	7	6	4
Indian	11	1	0
Latin American	0	1	0
Urban	3	12	8
Rural	10	20	19

TABLE 3

MONTH OF ONSET OF CASES OF TETANUS

	Neonatal	*Infants and children*	*Adolescents and adults*
January	1		
February		1	1
March		1	2
April	1	2	2
May	3	2	
June	2	5	3
July	1	3	4
August	1	6	5
September		6	3
October	1	6	3
November	2		2
December	1		2

children, adolescents, and adults has declined and a slight improvement in mortality has occurred. The case-fatality rate for nonneonatal tetanus for the period 1946-1950 was 34%; the rate for 1951-1963 was 25%.

Figure 2 demonstrates the age distribution of the patients studied and the number of deaths by age group. Sixty-six percent of the fatal cases occurred in neonates or children. The highest mortality was observed at the extremes of life; the case-fatality rate was 59% under 3 years of age and 80% for the group over 60 years of age.

The sex and race of the patients is shown in table 2. A preponderance of males is noted in all age groups but is most marked in the neonatal and adult groups. The racial origin of the patients is consistent with the makeup of this hospital's patient population with the exception of the larger number of Negro neonatal patients. Although 68% of injuries occurred in rural areas, only 6 patients, all farmers, had injuries related to their occupation. The vast majority of injuries were sustained in the course of daily living unrelated to occupational activities. Most of the injuries of children occurred while at play out-of-doors, frequently while going barefoot. Most of the adult injuries were sustained during activity out-of-doors unrelated to occupation, for example, while raking leaves or chopping wood.

The seasonal distribution of cases is shown in table 3. No seasonal aggregation of neonatal cases was observed. Both adult and childhood cases occurred year-around, but with highest incidence during the warmest months of the year. The cold weather cases were the result of burns, frostbite, and indoor injuries.

OBSERVATIONS ON CASES OF NEONATAL TETANUS

Twelve of the patients with neonatal tetanus had been delivered at home. Seven of these deliveries were attended by midwives, 2 by physicians, and 3 were unattended. One case followed delivery and circumcision in a hospital. In each case the umbilical stump was thought to be the site of infection, although tetanus bacilli could not be demonstrated in any. The initial signs in the 13 patients were as follows: dysphagia and feeding difficulty, 62%; trismus, 46%; and convulsions, 23%. Prognosis was related to the age of the patient on admission, which averaged 6.6 days for the fatal cases and 10.1 days for the survivors. On follow-up observation, 3 of the 4 survivors were found to have major central nervous system sequelae including mental retardation, spasticity, and convulsive disorders.

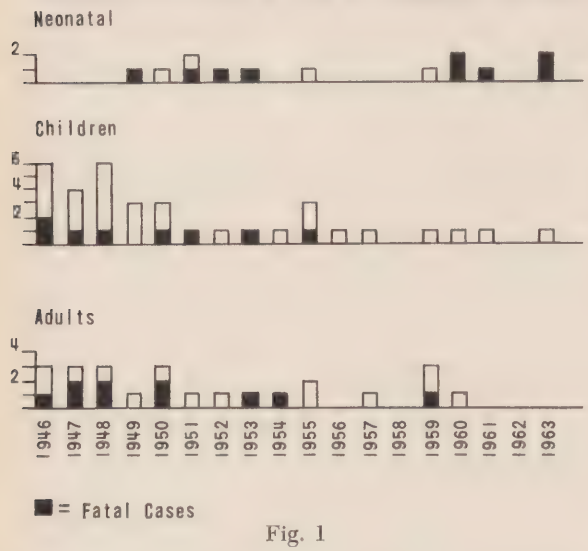


Fig. 1

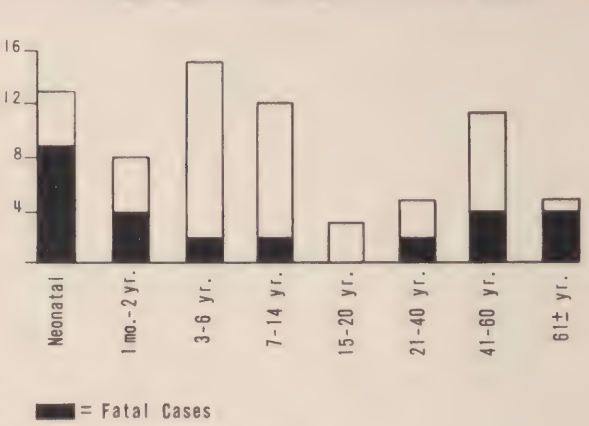


Fig. 2

OBSERVATIONS ON CASES IN INFANTS AND CHILDREN AND IN ADOLESCENTS AND ADULTS

Immunization status. The immunization status of the cases occurring in these age groups is presented in table 4. The case-fatality rate was higher for the totally unimmunized group (31%) than for the inadequately immunized group (12%).

Site and type of injury. The lower extremity was the site of injury in 70% of the patients in whom a wound could be identified. Puncture wounds or lacerations were found in 60% of the patients. The variety of injuries associated with tetanus in the remaining 40% is of interest (Table 5). In 10 of the 35 infants and children no injury could be recalled and no lesion could be demonstrated. Most of the injuries were considered by the patient to be trivial. Only 3 children and 8 adults consulted a physician at the time of injury. Of those who sought medical attention, only 1 child and 3 adults received adequate prophylactic treatment. Tetanus bacilli could be recovered from only 4 of the wounds.

Presenting complaints. Trismus was the most constant finding in adults, and the pattern of symptoms was fairly stereotyped (Table 6). In infants and children the initial symptoms were more variable. This variability of symptoms and the frequent absence of suspicious wounds contributed to a delay in diagnosis in several of the childhood cases.

Incubation period, severity, and mortality relationships. Incubation period for the infant-childhood and adolescent-adult cases ranged from four days to three months, but the majority of cases occurred within four to fourteen days of injury. The highest mortality rate was seen in the cases with an incubation period of seven days days or less (Table 7). No cases of "fulminant" tetanus were observed in those occurring beyond the neonatal period.

A direct relationship between severity of illness on admission and mortality was observed (Table 8). The mortality rate for clinically "mild" cases was quite low (6%). Three-fourths of the cases were classified as "moderate" or "severe" on admission. Overall mortality for this group was 40%, with the prognosis being better for infants and children than for adults. Cer-

TABLE 4

IMMUNIZATION STATUS OF CASES OF TETANUS

	Infants and children	*Adolescents and adults*
None	25	17
Inadequate	5	3
Complete	0	0
Not stated	2	7

TABLE 5

TYPE OF INJURY IN CASES OF TETANUS

	Infants and children	*Adolescents and adults*
Puncture	13	11
Laceration	4	7
Contusion-abrasion	3	2
Burn	0	3
Operation (tonsillectomy)	1	0
Otitis media	1	0
Arteriosclerotic gangrene	0	1
Blister	0	1
Wasp sting	0	1
Frostbite	0	1
No injury recalled	10	0

TABLE 6

PRESENTING MANIFESTATIONS IN CASES OF TETANUS

	Infants and children	*Adolescents and adults*
Trismus	41%	74%
Back and neck stiffness or opisthotonus	41%	19%
Local stiffness or spasm	16%	15%
Dysphagia	9%	15%
Generalized stiffness	3%	8%
Abdominal pain	6%	—
Irritability	6%	—
Generalized convulsion	3%	—

TABLE 7

RELATIONSHIP BETWEEN INCUBATION PERIOD AND MORTALITY

Incubation period	*Infants and children*		*Adolescents and adults*	
	cases	*deaths*	*cases*	*deaths*
<4 days	0	0	0	0
4-7 days	5	2	8	5
8-14 days	12	1	9	3
14 days	5	0	8	3
Unknown	10	3	2	1

TABLE 8

RELATIONSHIP OF SEVERITY OF ILLNESS AND MORTALITY

	Severity		
	Mild	*Moderate*	*Severe*
Infants and children			
Cases	8	18	6
Deaths	0	4	2
Case-fatality rate	0%	22%	33%
Adolescents and adults			
Cases	0	13	6
Deaths	1	7	4
Case-fatality rate	12%	54%	66%

TABLE 9

MORTALITY RATES IN RECENT SERIES OF TETANUS

Author	*Type of patient*	*Years*	*Mortality rate*
Howard and Riley*	Children and adults	1950-64	25%
Creech and associates[18]	Children and adults	1950-56	24%
Christiansen and associates[19]	Children and adults	1945-54	27%
Box[10]	Children	1956-62	9%
Altmeier and associates[16]	Children and adults	1947-58	21%
Kloetzel[9]	Brazilian children and adults	1962	35%
Tompkins[20]	African children	1953-58	31.6%

*Present report

tainly for adults, and to a lesser extent for infants and children, incubation period and severity of illness on admission are important guides to prognosis.

DISCUSSION

In 1959 in this country, 283 deaths due to tetanus were reported. Of these, 99 occurred in children less than 5 years of age and 32 in individuals 5 to 19 years of age. The majority of these resided in the southern and southeastern parts of the United States.[3] During the latter period of the present study, 1950-1964, the annual tetanus incidence in Oklahoma was 0.35 cases per 100,000 population, which was slightly higher than the national average. The high incidence of neonatal tetanus in the Negro and Latin American population of the South and Southwest has been pointed out in the excellent epidemiologic reviews of Axnick and associates[1] and of Health and associates.[2] Immunization with tetanus toxoid should be universal. This is true because tetanus occurs at all ages, and tetanus toxoid is among the most effective, yet innocuous, immunizing agents available. When used properly, its effectiveness approaches 100%, and the duration of immunity which it induces is strikingly lasting. That active immunization is effective seems clear from the experience in World War II among immunized United States and British personnel and the nonimmunized Japanese forces and also from the comparison of immunized and nonimmunized German troops. Military personnel received only primary tetanus-toxoid immunization followed by boosters at the time of injury. During the war, the United States Army reported more than 2,700,000 hospital admissions for wounds and injuries. Twelve cases of tetanus developed of which 6 were in men not properly immunized and 2 in troops who had not received boosters.[4] During the same period, there were 2,574 reported deaths due to tetanus among the civilian population in the United States.[5] In a nationwide survey conducted by the Bureau of the Census in 1962, four million children under the age of 5 years, 20% of those surveyed, had not received a single injection of diphtheria, tetanus, or pertussis vaccine. Of the white children, 18% were totally unprotected, whereas 31% of the Negro children had received no injections. The public apathy toward immunization must be overcome, and the vaccines must be administered to the population groups who need them. It is a strange paradox that 95% of the population of an area can be immunized with oral polio vaccine on a single day, and yet four million children under the age of 5 years have not been im-

munized against diphtheria, pertussis, and tetanus, although vaccines of proved effectiveness against these diseases have been available for many years. In all probability, the success of the oral polio vaccine program is due more to the participation of the medical profession at the local level than to the ease of administration.[6] Recent surveys have demonstrated the poor immunization status of adults, except those who were immunized during military service. It is a disturbing fact that 46% of females and 28% of males over 18 years of age have not had tetanus immunization, particularly with the availability since 1933 of tetanus toxoid, possibly our most satisfactory immunizing agent.[7] in view of the noteworthy incidence of both diphtheria and tetanus in the adult population, maintenance of immunity with periodic boosters of diphtheria-tetanus toxoid must be included as part of good preventive medical practice for adults as well as for children. With the exception of farmers, our series did not identify any "high-risk" occupation or avocation. This further emphasizes the necessity of adequate immunization for the entire population.

That the highest tetanus mortality occurs in the age groups at the extremes of life has been observed repeatedly.[8,9] Approximately 100 neonatal deaths from tetanus in the United States are reported annually, which is 25 to 35% of the total mortality from this disease. In our series and in that reported by Box,[10] none of the mothers of infants with neonatal tetanus had received any prenatal care. Recent studies of Schofield and co-workers,[11] have demonstrated the efficacy of maternal immunization in protection against neonatal tetanus. Recommendations for immunization of pregnant women in areas with primitive obstetrical practice have been made but are unlikely to influence the neonatal tetanus rate in this country. These observations suggest that improvement in the incidence of neonatal tetanus must await a general improvement in maternal care for the specific "high incidence" groups in this country. Although we have been unable to demonstrate any improvement in neonatal mortality in our small series, recent reports of 65 to 75% survival are encouraging.[10,12] At the other end of the life-span, even mild cases of tetanus may prove fatal to the elderly individual with marginal cardiorespiratory reserve, as was observed in our series. A particularly fulminant type of tetanus seen in narcotic addicts with mortality rates of 90 to 100% has been reported recently.[13,14] It is not clear whether this excessive mortality is due to the severity of the disease or to the poor general health of these individuals and complications of their addiction.

In our series, 29% of the children had no history of injury and no demonstrable lesion, while suspicious lesions were found in all adults. Recent series have reported no lesion in 10 to 50% of cases,[8,15–17] the higher rates being observed in cases occurring in infancy and childhood. Several authors have stressed the trivial nature of the wounds associated with most cases of tetanus. Box[10] observed that only 1 of 73 children in his series had been seen by a physician at the time of injury. Creech and associates[18] reported that only 1 patient in their series of 558 cases had received tetanus antitoxin at the time of injury. These observations emphasize the importance of maintaining tetanus immunity at an adequate level, since the physician is not likely to see the majority of patients at a time shortly after injury when prophylaxis with antitoxin or a booster of toxoid will be most beneficial.

Our mortality rate of 25% in children and adult tetanus cases is consistent with the experience of others (Table 9). Mortality for nonneonatal cases has declined from 34% of the 1946-1950 cases to 25% for the 1951-1963 cases in our series. The improved mortality could not be related to differences in use of antitoxin, tracheostomy, surgical excision of the wound, patient factors, or severity of disease on admission. Improved supportive medical and nursing care, including availability of antibiotics to control infectious complications, seems to account for this decrease in mortality. The reports of Kloetzel[9] and Box[10] discuss in detail the points in management of this disease and its complications. The long-term sequelae of tetanus were not studied in detail in our patients. However, at least 5 children were found in the immediate postacute period to have significant skeletal or nervous system sequelae, including 1 with a severe intellectual defect and a convulsive disorder, 3 with fractures or deformity of the thoracic spine, and 1 with a foot drop.

SUMMARY

Seventy-two cases of tetanus seen at the University of Oklahoma Medical Center from 1946 through 1963 are described from an epidemiologic and clinical viewpoint, and the pertinent literature on this subject are reviewed. The prognosis of neonatal tetanus continues to be poor, while that for nonneonatal disease is improving. Reduction in tetanus morbidity and mortality in this country awaits improvement in more universal immunization of both children and adults and in maternity care.

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Pulmonary Mucus in Cystic Fibrosis

Interrelationships with Pathogenic Bacteria

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THE PRESENT REPORT concerns experimentation designed to explore relationships between bacteria and pulmonary mucus in cystic fibrosis. The overall problem is whether these relationships are purely physical, physiological, or combinational between these factors. The approach was by a number of independent but correlated methods which included biochemical, immunological, and morphological studies. Emphasis was placed in areas in which information has been sparse, nebulous, or lacking.

MATERIALS AND METHODS

Mucus specimens. Three patients with proved cystic fibrosis were selected as subjects on the basis of cooperative attitude of the patients and their parents and the ability to produce copious mucus. One, a 5-year-old white female, was not under prophylactic antibiotic therapy. The second was a 9-year-old white male whose physician allowed withholding of drugs forty-eight hours, while specimens were being collected. The third, a 6-year-old white male, was on intermittent antibiotic therapy which permitted seventy-two hours of nontherapy, during which intervals specimens were collected. Nonfibrocystic secretions, for comparative control material, were obtained by suctioning the tracheostomy opening and trachea of an adult patient who had oral pharyngeal carcinoma and suffered intermittently from chronic bronchitis. This patient was not receiving antibiotic therapy. Specimens of mucus were diluted 1:4 with normal saline or distilled water. These materials were homogenized in an omnimixer, the receptacle of which was immersed in an ice bath. The homogenates were centrifuged, then filtered through bacteriologic filters. Many attempts were made to sterilize the whole mucus homogenates. The methods used were limited by the viscous nature of the material and by the need to maintain the natural state of the glycoproteins and glycopolysaccharides, without denaturation. In brief, no satisfactory method was found.

The concentrations of mucous materials in the saline and water extracts were estimated on the basis of quantitative protein determinations. Protein in pooled water extracts averaged 1.3 mg. per milliliter and in saline extracts, 2.2 mg. per milliliter. These extracts were further characterized by determinations of sialic acid and hexosamine content. The water extracts contained an average of 79.4 μg. per milliliter and the saline extracts 43 μg. per milliliter of sialic acid. The water extracts contained an average of 73.8 μg. per milliliter of hexosamine, whereas average content of the saline extracts was 51.6 μg. per milliliter of this material.

Microorganisms. Although a variety of strains of staphylococci were used in different phases of experimentation, the Emory strain of Staphylococcus aureus was the principal test organism employed. This is a hemolytic, coagulase-positive, phage type 80/81, penicillin-sensitive strain.

Two-dimensional tube dilution studies. The capability of the mucus extracts to protect bacteria from the effects of antibiotics to which they were otherwise sensitive was investigated by means of the two-dimensional tube dilution technique.[1] This method, which is diagrammatically illustrated in Figure 1, was originated to test the combinational effects of 2 antibiotics. In the present application, the usual 10 rows of 10 tubes each were arranged. Two-fold dilutions of penicillin starting with 50 units per milliliter were prepared and 1 milliliter of each dilution was placed in each tube of the horizontal row. Likewise, two-fold dilutions of the extracts were prepared, and 0.5 ml. was placed in each tube of each vertical row. Into each tube was placed 0.5 ml. of a 1:10,000 dilution of an eighteen-hour broth culture of the Emory strain of S. aureus, ordinarily sensitive to 6.25 units per milliliter of penicillin. If the extracts exerted any protective effect, this should have been evidenced in this setup by increased resistance to penicillin in the tubes containing the greater concentrations of

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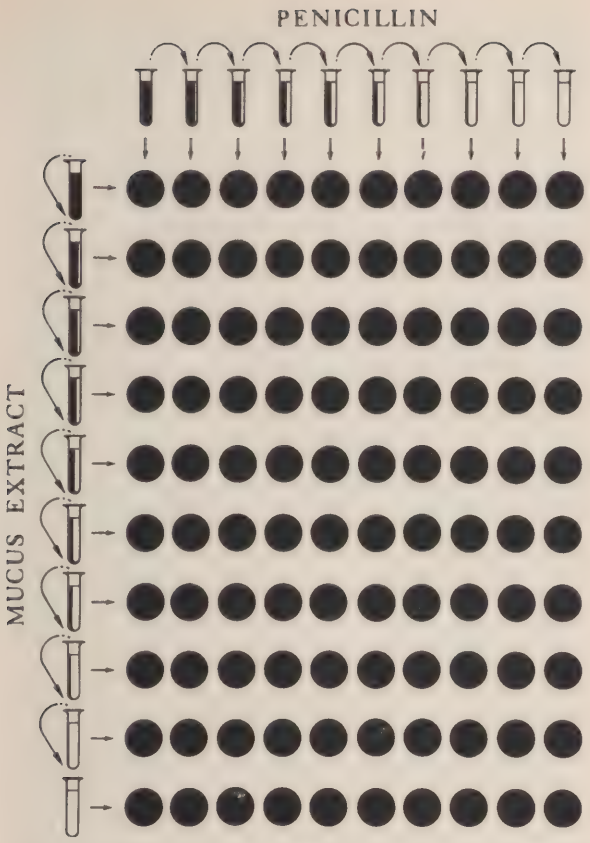


Fig. 1. Diagrammatic representation of two-dimensional tube dilution technique

extract. Thus, instead of an end point at the 6.25 unit per milliliter level, the growth pattern should have curved upward and to the left.

Immunologic studies. For immunologic studies, rabbit antiserums to the saline and to the water extracts were developed. These were found to be immunologically identical.

Comparisons were made by microimmunodiffusion techniques of the antigenic components of cystic fibrosis and chronic bronchitis extracts of mucus. Figure 2 illustrates a typical immunodiffusion plate.

The extracts were also immunologically checked for antistaphylococcal antibody content.

Portions of the rabbit anticystic fibrosis mucus extracts were conjugated with fluorescein isothiocyanate for fluorescent antibody comparisons between staphylococci incubated for eighteen hours in the presence of cystic fibrosis extracts and noncystic fibrosis extracts.

Electron microscopy. Samples of the same cultures were used for electron microscopic visualization of the apparent coating of the cells by the extract materials. In addition to the cultures incubated with fibrocystic and nonfibrocystic extracts, control cultures in brain-heart infusion broth were included for comparisons. All cultures were prepared for electron microscopy by centrifugation for two minutes at a relative centrifugal force of 700, and the supernates were discarded. Fixation was in 10% buffered formalin, followed by embedding in Maraglas. Sections were cut at 90 to 120 mμ.

RESULTS

Two-dimensional tube dilution technique. Not more than one tube differential in increased penicillin resistance could be demonstrated as protection by the mucus extracts in the two-dimensional tube dilution experiments. This differential was considered not to be significant.

Immunological studies. The comparative results of the microimmunodiffusion of fibrocystic mucus and nonfibrocystic extracts, using anti-fibrocystic extract antibody, are demonstrated in Figure 2. There appeared to be at least one antigenic component present in the fibrocystic mucus which was not present in the "normal" mucus, whereas another antigenic component appeared to be present in greater quantity in the "normal" mucus than in the fibrocystic mucus.

The micrographs in Figure 3 of the fluorescent conjugate-stained preparations of the staphylococci, grown in the presence of fibrocystic and of nonfibrocystic extracts of mucus, demonstrated clumping and specific staining of the staphylococci grown in fibrocystic extract. The preparations with "normal" extract showed no such results. The latter micrographs were exposed one minute longer and were overdeveloped, yet quite faint. The culture of the Emory strain of S. aureus grown in brain-heart infusion broth only, which was applied to each slide as a control, was stained so faintly it could not be photographed.

Electron microscopy. It was observed that thick material surrounded the S. aureus grown in the presence of fibrocystic mucus, as indicated in Figures 4, 5, and 6. The staphylococci which

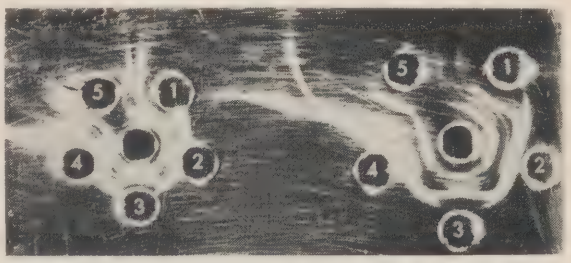


Fig. 2. Comparison of chronic bronchitis mucus extract to cystic fibrosis mucus extract by microimmunodiffusion. Contents of wells as follows: 1 and 3, chronic bronchitis mucus extract; 2 and 4, fibrocystic mucus extract; and 5 and center well, antiserum to fibrocystic mucus extract

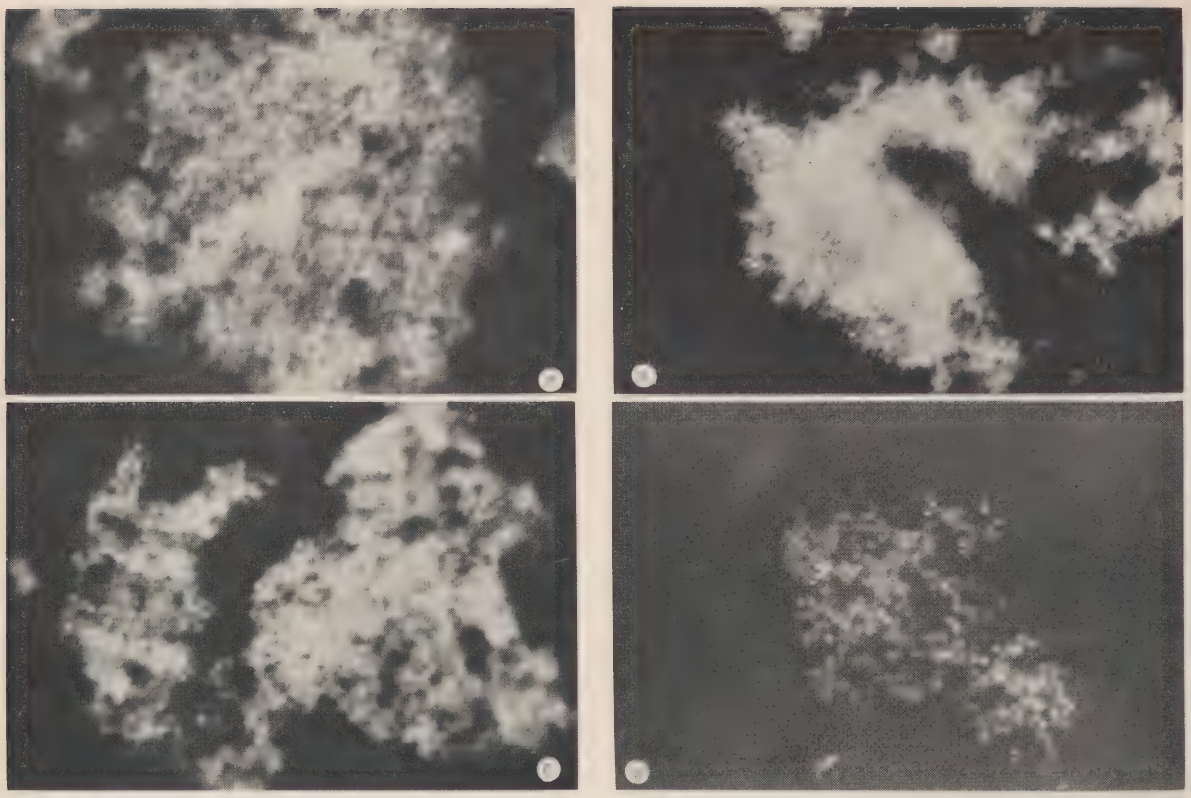


Fig. 3. Micrographs of fluorescent conjugate-stained preparations. Micrographs A, B, and C show fluorescent stained preparations of S. aureus grown in the presence of fibrocystic mucus extract. Micrograph D shows a stained preparation of S. aureus grown in the presence of chronic bronchitis mucus extract.

were grown in brain-heart infusion broth only and those grown in the presence of the extract of the mucus from chronic bronchitis showed no similar material surrounding them (Figs. 7 and 8, respectively).

DISCUSSION

It has been well documented that in only the tracheobronchial tree there is a peculiar host-parasite relationship between S. aureus and the fibrocystic patient. The key to this unusual ecological relationship appears to be the abnormal mucus produced in this site, which favors infection with coagulase-positive staphylococci. The use of antibiotics has lengthened the lifespan of fibrocystic individuals,[2–5] although the inability of the antibiotics to penetrate the mucus readily has been pointed out by many investiga-

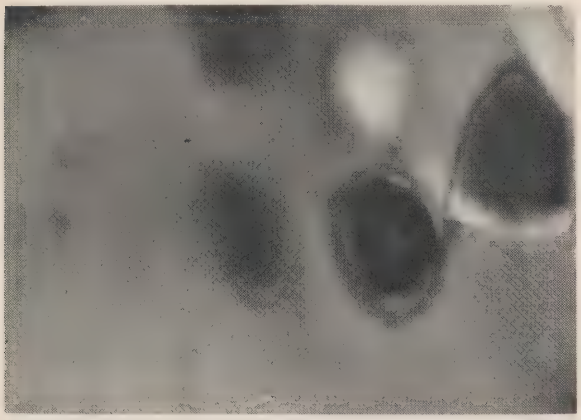


Fig. 4. Electron micrographs of S. aureus grown in the presence of fibrocystic mucus extract (formalin fixation, × 52,800)

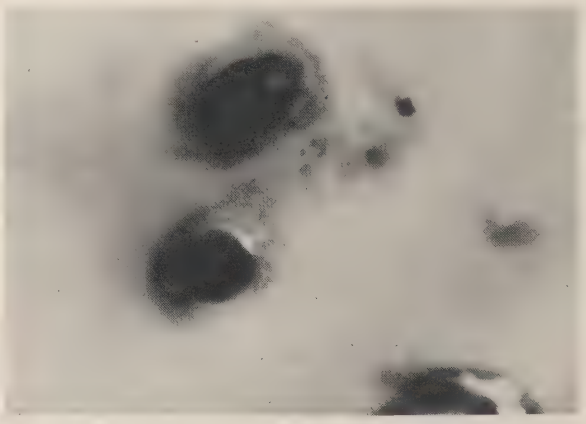


Fig. 5. Electron micrographs of S. aureus grown in the presence of fibrocystic mucus extract (formalin fixation, × 52,800)

tors.[6,7] The question which presents itself is why S. aureus is so constantly associated with the bronchial secretions of the fibrocystic patient. Why is it that antibiotic therapy is empirically successful yet does not effectively reduce infection with S. aureus or cause the exchange of one phage type for another, except in long-term therapy? Many of the investigators dealing with these problems have proposed that the principal consideration is the fact that antibiotics are unable to penetrate the mucus.[6,7] Pathologists report commonly seeing at the necropsy of a fibrocystic patient clumps of bacteria enclosed in mucus secretions in the bronchioles.[7] One of the principal objectives of the present work was to study this association between staphylococci and the tracheobronchial secretions of cystic fibrosis. A primary objective in approaching this problem was to find a representative substance with which to create valid experimental conditions. The attempts to sterilize whole homogenates of mucus were toward this end, but failure to achieve sterility precluded their use in pure culture techniques. (The fact that the bacterial flora could not be killed demonstrated the great barrier the mucus presents in vitro.) Water and saline extracts were attractive alternatives because it was not likely that their addition to the mucus would denature the material. The products could be sterilized by filtration, thus allowing the use of pure culture techniques, and could be added to bacterial cultures safely, which would not be true of the products of certain other solvents. Furthermore, workers have reported[8–12] the use of saline or water solutions in successful mucus extraction procedures. The high hexosamine and sialic acid contents lend credence to the assumption that at least a sizable fraction of the fibrocystic mucus was extracted by the water or saline treatment.



Fig. 6. Electron micrographs of S. aureus grown in the presence of fibrocystic mucus extract (formalin extract, × 52,800)

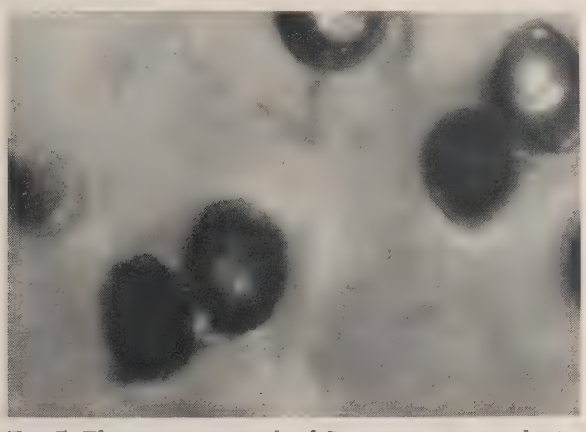


Fig. 7. Electron micrograph of S. aureus grown in brain-heart infusion broth (formalin fixation, × 52,800)

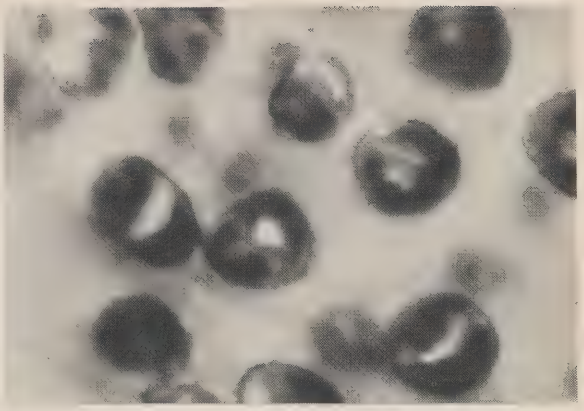


Fig. 8. Electron micrograph of S. aureus grown in the presence of chronic bronchitis mucus extract. (formalin fixation, × 52,800)

The apparent failure of the two-dimensional tube dilution technique to demonstrate a sequestering of the bacterial cells from the action of penicillin may have been due to the considerable dilution of the extracts or to the fact that they were incomplete, lacking the thick viscid portions of the whole specimens. High[13] reported that he has studied antibiotic levels in nonfibrocystic bronchial secretions and found only trace amounts present when the serum drug levels were high. It would thus appear that the primary effect of whole mucous secretions with regard to chemotherapeutic agents is mechanical, rather than physiological. Whether the antibiotic does not pass the mucous membrane readily or antibiotic diffusion is inhibited in mucous secretions, the site in the body at which the antibiotic activity is most effective is probably the lung tissue, rather than the lumina of the tracheobronchial tree. This could explain the clinical success of short-term antibiotic therapy which does not disturb the flora.[7] If an invasion of the lung tissues began, the mucus would be absent and the tissue level of the antibiotic would be sufficient to curb

the invasion. As long as the bacteria were sequestered in the bronchioles by the mucus, however, the antibiotic could not reach the bacterial cells in a concentration great enough to affect them or change the flora. The antigenic differences demonstrated by microimmunodiffusion between the nonfibrocystic and fibrocystic mucus extracts may be due to the actual absence of certain antigenic determinants from the nonfibrocystic preparation or due to their presence in undetectable amounts. The nonfibrocystic extract appears to contain some fraction in greater quantity than the fibrocystic extract. This could be due to many factors, possibly linked to the moribund state of the patient from whom nonfibrocystic mucus was obtained. The rabbit antifibrocystic mucus antibody was considered to be quite specific, especially in view of the strikingly positive staining by the fluorescent antibody of the staphylococci grown in the presence of the specific extract of mucus. The type of bacterial growth in the presence of fibrocystic extract is quite different from that in nonfibrocystic extract. The protein contents of the two are very similar and would not appear to be a factor. It has been postulated that bacteria may incorporate foreign antigenic materials into their own cell walls. Kaplan[14] believes that he has found this too true of streptococci grown in broth containing heart infusions. The antigenic materials appear to be incorporated into the cell walls and are then capable of reacting with specific host-derived antiserums. It is conceivable that the staphylococci in the lumina of the tracheobronchial tree of the fibrocystic hosts are actually incorporating host products into their own cell walls. This could account for the positive staining by the fluorescent conjugate of the staphylococci grown in the presence of the extract. If this were true, it could partially account for the inability of the body to defend itself with normal immune and phagocytic mechanisms against staphylococci in the bronchial tree. Even a simple coat of the mucus of the host could act in the same manner to defend the staphylococci from the host. In effect, the staphylococci present in patients with cystic fibrosis may incorporate elements of mucous secretions into their cell walls, thus gaining the password for unchallenged admission to the patient's tissues. A vigorous immunologic defense by the host would not be elicited, and the bacteria could thus become well entrenched. Perhaps this can partially explain why patients are susceptible to staphylococci only in the tracheobronchial tree, for only active growth at this site could provide incorporation of the host's own mucous products; after multiplication at other sites in the host's body, these would be lost. Electron microscopy was utilized to clarify the relationship between S. aureus and the mucus in which it was grown. It was hoped that this might distinguish between coating of the cells and actual incorporation into the cells of mucous material or, perhaps, indicate some cause for the clumping of S. aureus grown in the presence of fibrocystic mucus. Staphylococci grown in extracts of mucus did not demonstrate "encapsulation" when viewed by light microscopy. The electron micrographs appear to show specific coating, but it is questionable whether or not actual intracellular incorporation of the material can be discerned. It is interesting to note that very similar electron micrographs of Pseudomonas in the presence of fibrocystic mucus have been presented recently.[15]

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Coexistent Cranial and Spinal Defects with Hydrocephalus in Five Infants

The Etiology and Significance of Craniolacunia in These Defects

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THE INCIDENCE OF malformations of the central nervous system varies from 5 to 8 per thousand births.[1–3] Of 200 consecutive patients with central nervous system malformations examined at the Children's Memorial Hospital, 5 presented with a combination of 3 defects: hydrocephalus, cranial defects (craniolacunia, craniofenestra, or cranial meningocele), and spinal defects (meningocele or meningomyelocele). Although such defects occur singly, the coexistence of spinal and cranial defects and hydrocephalus in the same patient has been reported only rarely.[1,4–8]

CASE REPORTS

Case 1. S.A., a 7-day-old white female, was admitted to the Children's Memorial Hospital with a meningomyelocele and frontal bone protrusion. She was delivered by cesarean section of a gravida II, para II mother at eight months' gestation, immediately after the mother sustained a fall which resulted in excessive uterine bleeding. The infant weighed 6 lb. 8 oz. and appeared normal except for the spinal defect. Family history revealed that a second cousin expired one year previously at the Children's Memorial Hospital of hydrocephalus with meningomyelocele.

Physical examination revealed a small, active infant with an obvious protrusion of the forehead (Fig. 1a). The occipitofrontal circumference was 32.5 cm. and there was a small 3 × 3 cm. thoracolumbar meningomyelocele covered with a green exudate. The frontal bone protrusion measured 2 × 2 cm. and did not transilluminate. Hypesthesia, hypalgesia, decreased tone of the lower extremities, and clubfeet were present.

Lethargy, poor feeding, and temperature elevation occurred on the fourteenth day, and laboratory study confirmed the diagnosis of purulent meningitis. Escherichia coli was isolated from the cerebrospinal fluid and Staphylococcus aureus from the meningocele. Despite intensive therapy, the infant expired within twenty-four hours.

Case 2. B.T., a 2-day-old white male, was admitted to the Children's Memorial Hospital with a meningomyelocele and a large frontal bone protrusion. He was delivered spontaneously from a gravida I mother who experienced no complications during the pregnancy. The infant weighed 8 lb. 12 oz. Similar malformations in the family were not recorded.

Physical examination revealed an active infant with a large 5 × 8 cm. thoracolumbar meningomyelocele and a 4.5 × 4.5 cm. frontal cranial meningocele which did not transilluminate. The occipitofrontal circumference was 39.5 cm. and the chest circumference was 32.5 cm. (Fig. 1b). Other anomalies included a preauricular ear tag and hypesthesia, hypalgesia, and hypotonia of the lower extremities without clubfeet.

The infant did well during the first fourteen days of life without evidence of infection. He was discharged to the Children's Convalescent Hospital to be readmitted at a later date for surgical repair of the meningomyelocele. At 5 weeks of age, he developed progressive lethargy and fever, refused feeding, and was readmitted with purulent meningitis. The cerebrospinal fluid was cloudy and culture yielded Proteus organisms. The infant expired shortly after admission.

Case 3. I.M., a 1-day-old Indian female, was admitted to the Children's Memorial Hospital with a frontal protrusion and lumbar meningocele. She was the result of a spontaneous delivery of a gravida II, para II mother whose pregnancy was complicated during the third month by an episode of diarrhea. The infant was delivered from a brow presentation, weighed 5 lb. 10 oz., and had an Apgar score of 5. The neonatal period was uncomplicated. There was no family history of malformations of the central nervous system.

Physical examination revealed a small, active infant with an obvious frontal bone protrusion which measured 2 × 3 cm. The underlying frontal bone was absent and one was able to palpate the meninges and underlying brain. The occipitofrontal circumference was 35 cm. and the chest circumference 33 cm. There were also a 5 × 5 cm. thoracolumbar meningomyelocele and bilateral clubfeet with hypesthesia, hypalgesia, and hypotonia of the lower extremities (Fig. 1c).

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Fig. 1a. Case 1. Frontal bone protrusion (craniofenestra) and small lumbar meningomyelocele





Fig. 1b. Case 2. Cranial meningocele in frontal bone and large thoracolumbar meningomyelocele





Fig. 1c. Case 3. Cranial meningocele in frontal bone and large thoracolumbar meningomyelocele



Fig. 1d. Case 4. Occipital meningocele and thoracolumbar meningomyelocele and clubfeet



Fig. 1e. Case 5. Frontal protrusion, cranial meningocele, and large thoracolumbar meningomyelocele

The child did well the first two days of life and then developed poor feeding and lethargy and had an episode of apnea. Lumbar puncture revealed cloudy purulent spinal fluid from which Pseudomonas aeruginosa was isolated. Despite intensive therapy of the meningitis, the infant expired within twenty-four hours.

Comment. This infant and Case 2 are similar to Case 2 of Rothbart[5] and Case 5 of Van Waalwijk von Doorn.[6]

Case 4. P.N., a white female, was admitted to the newborn service with multiple anomalies, including a spinal meningomyelocele and an occipital meningocele. She was the product of a full-term pregnancy in a gravida V, para V mother who received an injection of an unknown drug in an attempt to produce an abortion between the third and fourth weeks of gestation. She developed toxemia during the eighth month of pregnancy. The labor was nine hours, and the infant was delivered spontaneously from a left occipital anterior position. The Apgar score was 6, and she weighed 7 lb. 4 oz. Family history revealed 2 infants with malformations. A first cousin of the infant had renal hypoplasia, and another cousin had a ventricular septal defect of the heart.

Physical examination revealed an active, obviously malformed infant with an occipitofrontal circumference of 34 cm. The chest circumference was 33 cm. A thoracolumbar meningomyelocele measuring 3×7 cm. and an occipital cranial meningocele 6×7 cm. were present (Fig. 1d). Other anomalies included a high arch palate, microphthalmus, bilateral clubfeet, and small, spindly lower extremities with flaccidity, hypalgesia, and hypesthesia.

On the sixth day of life, she began to have apnea. Although meningitis and sepsis were strongly suspected at this time, the cerebrospinal fluid was normal. The child was given intensive antibiotic therapy and improved during the next two weeks but expired on the twenty-eighth day of life.

Comment. A similar case is radiologically demonstrated by Vogt and Wyatt[7] in a study of craniolacunia.

Case 5. A.B., a 7-day-old white female, was admitted

TABLE 1

CLINICAL FEATURES IN COEXISTENT MALFORMATIONS OF CENTRAL NERVOUS SYSTEM

Case	Sex	Age in days	Circumference in centimeters		Location and size in centimeters		Associated defects
			Head	Chest	Spinal defect	Cranial defect	
1	F	7	32.5	28.5	Lumbar 3×3	Frontal 2 × 2	Clubfeet
2	M	2	39.5	32.5	Thoracolumbar 5×8	Frontal 4.5 × 4.5	Preauricular
		35	43.0				Ear tag
3	F	5	35.0	33.0	Thoracolumbar 5×5	Frontal 2 × 3	Clubfeet
4	F	2	34.0	33.0	Thoracolumbar 3×7	Occipital 6 × 7	High arch palate
		28	36.0	33.0			Microphthalmus
5	F	7	35.0	28.0	Thoracolumbar 6×7	Frontal 2.5 × 2.5	High arch palate
		30	38.0	31.0			

to the Children's Memorial Hospital because of spinal and cranial meningoceles. She was delivered of a gravida II, para II mother, whose pregnancy was complicated by tonsillitis at three months, pyelonephritis at five months, and toxemia at six months. An elective cesarean section was performed because of a breech presentation. The infant weighed 5 lb. 6 oz. She developed respiratory difficulty during the first day of life and had an episode of cyanosis, five minutes in duration. The family history revealed that a sister had multiple hemangiomas of the face and chest and a cousin had a "cerebral palsy" syndrome.

The physical examination revealed a small, lethargic infant who had obvious deformities of the spine and skull. The occipitofrontal circumference was 35 cm. and the chest circumference was 28 cm. A thoracolumbar meningocele measuring 6 × 7 cm. and a 2½ × 2½ cm. frontal cranial meningocele were present (Fig. 1e). The infant had a high arch palate and clubfeet. The lower extremities exhibited flaccidity, hypotonia, hypalgesia, and hypesthesia.

On the tenth day of life, the infant developed progressive lethargy with episodes of apnea. A ventricular tap was performed and clear ventricular fluid without cells and with a negative culture was obtained. Despite antibiotic therapy, the infant expired at 30 days of age from a suspected sepsis.

Clinical features. The clinical features of these infants are illustrated in Figures 1a to 1c. The size of the cranial and spinal defects varied. The limb defects of flaccidity and clubfeet were similar to those illustrated in Figure 1d (Case 4). Table 1 records the ages when the infants were first seen and the discrepancies observed in occipitofrontal circumference and chest circumference. Although sizes of the spinal and cranial defects were variable, characteristic features of meningocele and meningomyelocele were noted (Figs. 1a to 1c). The spinal defects in all patients were thoracolumbar or lumbar in location and very extensive except for one 3 × 3 cm. defect of the lumbar region. Four of the cranial defects were located in the midline frontal region; in one patient, it was in the occipital area. Transillumination of the head was increased only in the occipital cranial defects. Other anomalies observed in these infants included high arched palate, accessory ear tags, microphthalmus, and secondary limb deformities such as clubfeet (Table 1).

Roentgenographic features. Figures 2a to 2e demonstrate craniolacunia, frontal and occipital cranial defects, and spinal defects. The roentgenograms of the skull confirmed the round, smooth protrusions which were palpable in the frontal, parietal, and occipital regions and which represented craniolacunia. On the other hand, the frontal and occipital defects of craniofenestra and cranial meningocele were evident by palpation of the large bony defect demonstrated by the roentgenogram. Underlying meninges and brain were easily palpated through the areas of defective bone. No roentgenograms were obtained in Case 3. The vertebral defects varied in extent and severity from scoliosis and marked gibbus to neural arch defects with fusion of the vertebrae. All of the lumbar, thoracolumbar, and cranial defects were associated with early development of hydrocephalus. In 3 of the infants who had ventricular taps for cerebrospinal fluid studies, the needle was inserted less than 2 cm. through the coronal suture. In 1 infant, Case 5, 10 cc. of air were instilled during the procedure, and roentgenograms of the skull at this time revealed moderate ventricular dilatation (Fig. 2e).

Etiologic factors. All patients were studied intensively for possible etiologic factors. In 1 infant, Case 4, 2 maternal aunts had children with congenital anomalies. One child had congenital renal hypoplasia and the other a ventricular septal defect. Another infant, a second cousin of Case 1, had a meningomyelocele with hydrocephalus. A sister of Case 5 had multiple cutaneous hemangiomas, while a cousin had a "cerebral palsy" syndrome.

Because of the association of medication in congenital malformations, detailed inquiry of drugs taken during the first four months of pregnancy with these infants was conducted.

TABLE 2

AGE OF ONSET OF BACTERIAL COMPLICATION AND DEATH WITH BACTERIOLOGIC STUDIES

Case	Sex	Age onset (days)	Days before expiration	Ventricular or cerebrospinal fluid studies	Organism isolated	
					Cerebrospinal fluid	Meningocele
1	F	14	1	Cloudy purulent fluid	Escherichia coli	Staphylococcus aureus
2	M	35	1	Cloudy purulent fluid	Proteus	None
3	F	5	1	Cloudy purulent fluid	Pseudomonas aeruginosa	Pseudomonas aeruginosa
4	F	6	22	Xanthochromic fluid No cells	None	None
5	F	10	30	Clear fluid	None	Alpha streptococcus

Appetite depressants, tranquilizers, antibiotics, vitamins, and mineral preparations were frequently used during this period. The mother of Case 4 received at four weeks' gestation an unknown type of abortifacient.

Upper respiratory infections, pyelonephritis, and bronchopneumonia occurred during the first trimester in two of the mothers.

Two of the 5 mothers were not married at the time of conception and another mother did not know the father of her child. Three mothers were from low socioeconomic levels. There were 4 female infants and 1 male infant born in April, May, August, October, and December 1962, respectively. One was an American Indian and 4 were Caucasian.

Chromosomal studies of 1 infant (Case 4) revealed a normal karyotype with 46 chromosomes. (This was performed by Dr. K. Dumars, Cytogenic Laboratory, Penrose Hospital, Colorado Springs, Colorado.)

Laboratory studies and complications. Table 2 lists pertinent data relative to infections which led to eventual death of the infants. Meningitis secondary to gram-negative organisms resulted in death within twenty-four hours in 3 of the infants (Cases 1 to 3) in spite of vigorous antibiotic therapy. Sepsis occurred in the other 2 infants (Cases 4 and 5). Infection was obviously related to the open spinal defect.

Autopsy studies. Neuropathologic studies of one infant (Case 1) revealed hydrocephalus secondary to an Arnold-Chiari malformation with aqueductal stenosis. External examination of the brain revealed flattened gyri and narrow sulci. The parietal and occipital lobes had numerous microgyri. The base of the brain was covered with gray, purulent exudate, which partially obliterated the basal cistern and interpeduncular fossa. There was only one dysplastic cerebellar hemisphere. On coronal section, the lateral ventricles were markedly dilated and the septul pellucidum was completely obliterated. The third ventricle was moderately dilated and extended to a narrow, forked aqueduct. The fourth ventricle was small but normally constituted. The diagnosis was obstructive hydrocephalus due to aqueductal stenosis with marked ventricular dilatation and bacterial meningitis.

Treatment. Although intensive antibiotic therapy was instituted with the early signs of infection, medical treatment was ineffective. Neurosurgical correction of the spinal defects also did not seem possible because of the size of the defects and the presence of other anomalies in the patients.

DISCUSSION

Development of hydrocephalus. An increase in head circumference may be a late manifestation of hydrocephalus associated with lumbar meningomyelocele. Frequently, ventriculography or pneumoencephalography reveals ventricular dilatation before the appearance of suture separation, setting-sun phenomenon, or increased head circumference. In previous studies, hydrocephalus has developed in 80% of infants.[7,8] Hydrocephalus in the present series was associated with Arnold-Chiari malformation, aqueductal stenosis, and impaired absorption of cerebrospinal fluid due to meningeal infection. Studies confirming the association of spinal defects with hydrocephalus have been made; however, correlation of the cranial defects with development of hydrocephalus and other complications has not been stressed.[4,7,9] In order to clarify the significance of cranial defects (craniolacunia), a review of the observations and studies of several European and English investigators is presented.[5–7] The clinical significance of the cranial defects accompanying spinal defects and hydrocephalus is discussed because the etiologic factors of malformation of the central nervous system and craniolacunia may be related.

Craniolacunia, craniofenestra, and cranial meningocele. Craniolacunia (luckenschädel, lacunar skull), an abnormality of fetal and newborn

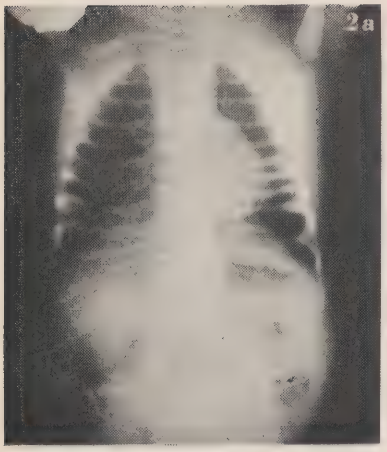




Fig. 2a. Case 1. Cranial meningocele with frontal protrusion and thoracolumbar vertebral defects

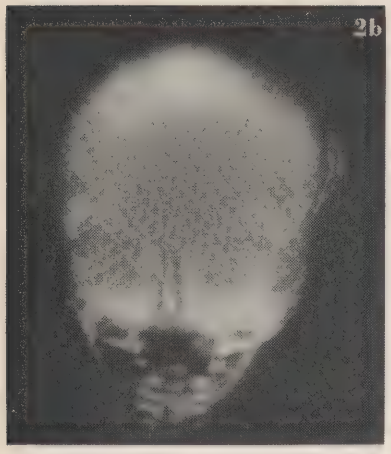




Fig. 2b. Case 2. Lateral and anteroposterior roentgenogram of skull demonstrating craniolacunia and cranial meningocele

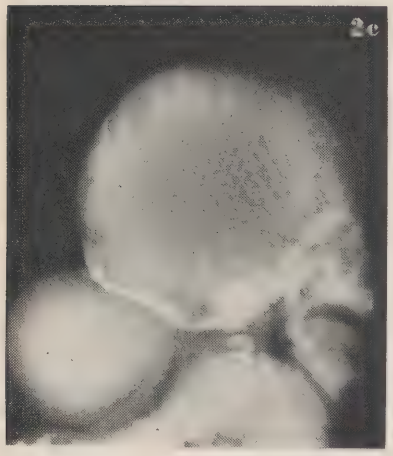




Fig. 2c. Case 4. Lateral skull and spinal roentgenogram with marked craniolacunia throughout, occipital meningocele, and vertebral anomalies

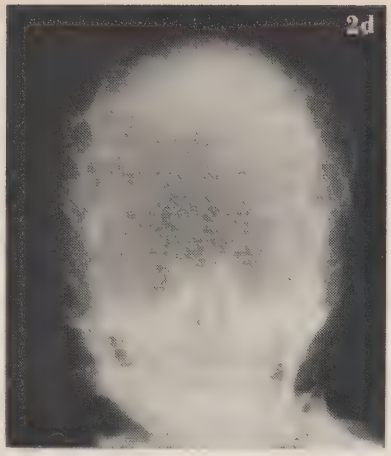
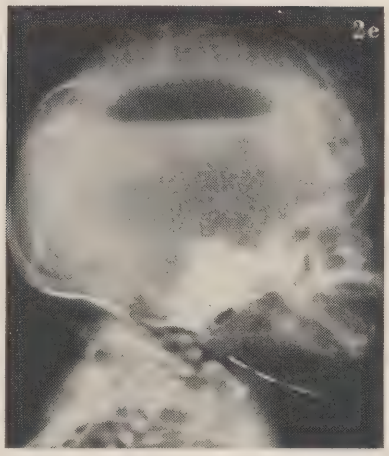




Fig. 2d. Case 5. Anteroposterior skull roentgenogram demonstrating craniolacunia and anteroposterior roentgenogram of spine demonstrating neural arch defects and scoliosis



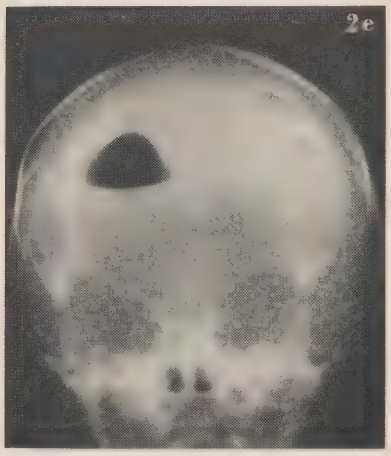


Fig. 2e. Case 5. Posteroanterior and lateral skull roentgenogram demonstrating enlarged ventricles

skulls, is a netlike arborizing pattern of bony ridges sharply delineated and separated by small, round defects of the inner table of the cranium.[5–7] First described in 1874 by Hoffman[10] and by West[11] in 1875, it is easily recognized during late stages of pregnancy and in the newborn period by the roentgen appearance of the skull.[12–20] When the skull is pathologically and radiologically examined, thinned areas appear translucent and are bordered by thick, interlacing ridges of bone. These ridges are no thicker than the normal bone, but they appear thicker because of the intervening zones of rarefaction.[6,7] Commonly present in the frontal and parietal portions of the skull, they may also be palpated in the occipital bone.[21]

Craniofenestra is a true palpable defect of the inner and outer table of the skull. These defects in the frontal, parietal, and occipital areas are of variable size, and cerebral structures do not protrude through the defect.[6] In contrast, cranial meningocele like spinal meningocele, is a midline, bulging defect composed of skin and meninges. The defect usually appears as a frontal or occipital pouch. If cerebral structures are found within the pouch, an encephalocele is present.[21]

Undoubtedly, these cranial defects represent varying manifestations of dermal, meningeal, and bony defects. Thus, the mild defects would comprise craniolacunia, in which severe abnormalities may be expressed as cranial meningocele or encephalocele. Certainly, the terms multiple encephalocele, relief skull, and basket skull should be discarded in favor of these terms which designate the cranial defects according to structural alteration.[6,21]

Although the cause of craniolacunia is not known, early reviews by several investigators have suggested plausible etiologic factors.[22–29] Three theories have been advanced: [1] increased intracranial pressure, [2] primary disturbance of ossification of the skull, and [3] association with disease.[5]

During the fourth to ninth months of fetal

TABLE 3

MALFORMATIONS AND OTHER DISORDERS ASSOCIATED WITH CRANIOLACUNIA

Author	Number of cases	Associated defect
Vogt and Wyatt[7]	53	Meningocele, hydrocephalus
Hartley[28]	28	Encephalocele, hydrocephalus, or meningocele
Ziemnowicz[4]	18	Spina bifida, hydrocephalus
Rothbart[5]	8	Myelomeningocele
Von Waalwijk van Doorn[6]	5	Cranial and spinal meningocele, encephalocele, Mongoloid facies, clubfeet, cleft palate
Durand[31]	1	Absence of septum pellucidum, spina bifida
Shopfner, Jabbour, and Vallion[30]	83	Cranial and spinal meningocele, encephalocele, hydrocephalus

development, the brain grows faster than the skull. The delay in development of the skull is completely physiological, sometimes leading to appositional defects with softening chiefly along the parietal suture margins. Such defects may be found in 25% of all newborn babies. The bone is thin and lacking in osseous development, while the adjacent bone is normal. This is termed "weichschädel" (craniotabes) and should not be confused with lacunar skull.[21,23–25]

When a meningocele is present, abnormal hydrodynamics result in a closer adherence of the brain to the skull. In some instances, postmortem studies relate the pressure changes in the skull to the convolutions of the brain and the location of the lacuna. There is a general, though vague, semblance of a convolutional pattern. Several cases of microgyri, flattened gyri, and cortical atrophy, however, have been associated with craniolacunia, but size relationships of the gyri to the lacuna have not been observed.[5,6]

Other investigators have attributed the lacuna to secondary pressure changes which cause ischemia by interference of the vascular supply. This concept has received further support from observations of an abundant vascular supply to the ridges of lacuna.[17,25]

Several earlier studies[5,6,24,25] proposed a primary defect in ossification related to the following factors: [1] disturbance of ossification due to abnormal pressure, [2] congenital hypostosis, and [3] congenital metabolic developmental imperfection. A primary developmental defect probably exists because of the associated bony, cerebral, and multiple anomalies.[5,6,15,16] Undoubtedly, several factors are related to these abnormalities. For instance, maternal disease or nutritional deficiency was recorded in several infants with lacunar skull and multiple anomalies.[6,22,28] The increased incidence of lacunar skull in the lower socioeconomic strata and during periods of food deprivation in Europe during and after World War II also suggests this causal relationship.[6]

During normal development of the skull, there is a process of intramembranous bone formation that is primarily dependent upon a constant, metabolic, vascular hemeostasis and secondary pressure growth stimuli that are genetically determined.[28] In the studies of the lacunar skull, several deviations from the homogenous bony development of the normal skull have been observed.[6] Thickening of the skull occurred near the dural vessels, while marked thinning of the skull occurred distal to the vessels.[29]

The possibility of a developmental defect, not only in the primitive membranous skull (mesoderm) but also in the spinal and dermal structures (ectoderm), strongly suggests an inherent genetic defect in which dysplastic mesoderm predominates and thus gives rise to multiple defects. Several infants similar to the present ones with multiple congenital defects of both mesodermal and ectodermal origin associated with craniolacunia strongly support this concept of a tissue or metabolic dysplasia (Table 3).

Several possible alterations associated with craniolacunia are listed in Figure 3. Needless to say, further investigative studies of nutritional, vascular, osseous, hereditary, and developmental aspects must be conducted. Each inciting stimulus must be evaluated with the other. Then, the initial stimulus, genetic or otherwise, must be determined. It is likely that multiple factors superimposed on an existing hereditary predisposition of malformations may explain the varying degrees of these cranial and spinal defects

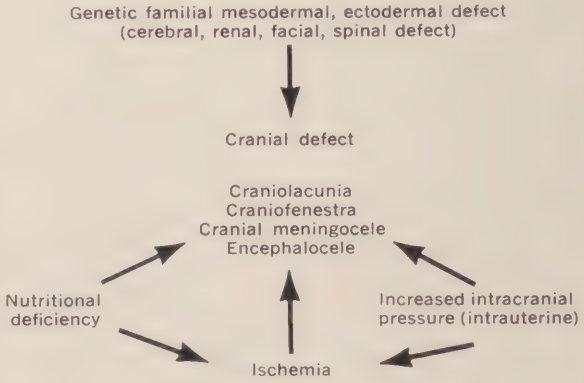


Fig. 3. Probable etiologic and pathophysiologic mechanisms in coexistent malformations

and possibly the coexistent malformations of the central nervous system.[28]

Clinical significance of craniolacunia and craniofenestra. In a study of the clinical significance of craniolacunia in a series of 102 infants with meningoceles, Vogt and Wyatt[7] rated the clinical responses of patients as: [1] good, those patients with normal mental development without disabling or neurological abnormalities, [2] fair, those patients with mild neurological residual but otherwise normal, [3] poor, those patients with obvious mental or physical disability, and [4] dead, 30% of the group. Of the patients in the "good" category, only 2 of 19, or 10%, had craniolacunia. Fourteen, or 64% of 22 patients, rated "poor" had craniolacunia. Thirty-five patients died and 57% of these had craniolacunia. Follow-up on 28 patients was not possible, although 54% of these patients had craniolacunia. It is obvious from these figures that patients who had craniolacunia as part of their disorder did poorly. Forty-eight percent of the patients with craniolacunia developed progressive hydrocephalus, whereas 25% of those without craniolacunia developed hydrocephalus. Thus, craniolacunia must be appreciated fully by first being aware of its presence and the poor prognosis which it signifies. Recent studies of 18 cases of spinal defect with craniolacunia and craniofenestra by Ziemmowicz,[4] as well as the patients in the present series, also confirmed this finding. These findings have been observed in a series of infants recently reported.[30] Further studies of earlier and serial roentgenograms of the skull in infants must be carried out in order to correlate the cranial defects and the prognostic significance.

SUMMARY

The clinical, roentgenographic, and etiologic factors in five infants with varying cranial defects (craniolacunia and craniofenestra or cranial meningocele), hydrocephalus, and spinal defects (meningocele or myelomeningocele) are described. All of the infants expired of bacterial complications. The etiologic factors and significance of cranial defects in these coexistent malformations of the central nervous system are reviewed.

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Anicteric Erythroblastosis

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THE MAJOR CONTRIBUTIONS to our understanding of erythroblastosis date back to 1910 when Schridde[1] described extensive extramedullary hematopoiesis, chiefly erythroblastotic, accompanying universal edema of the fetus. In 1912, Rautmann[2] termed the underlying condition responsible for universal edema of the fetus "erythroblastosis." In 1932, Diamond, Blackfan, and Baty[3] concluded that congenital anemia of the newborn, familial icterus gravis neonatorum, and universal edema of the fetus are dependent on the same underlying pathological process and regarded them as manifestations in the natural sequence of that disease. Since that time the 3 entities have been regarded collectively as erythroblastosis fetalis.

Erythroblastosis fetalis is traditionally considered a disorder characterized by the presence of jaundice secondary to an acquired hemolytic anemia. Although hemolysis and anemia are fundamental abnormalities of the disorder, hyperbilirubinemia and jaundice, at least in recent years, have dominated the thinking of most clinicians who are concerned with erythroblastosis. Anemia without jaundice may be the presenting and only clinical feature of this isoimmunologic process in the newborn and it is the purpose of this report to cite several occurrences of anicteric erythroblastosis.

CASE REPORTS

Unusual clinical courses have been observed in the erythroblastotic infants of 2 families. These infants had hemolytic anemia without hyperbilirubinemia. The affected infants in these 2 families present the salient features of anicteric erythroblastosis, namely mild or no jaundice in the face of active hemolysis.

Other causes of congenital anemia could not be found. None of the affected infants had history or findings suggestive of posthemorrhagic anemia. This is supported by the fact that anemia without jaundice occurred in successive siblings in each family. All infants were delivered at or after thirty-seven weeks gestation without apparent complications of parturition. All of these infants are now living and well.

Family 1. The maternal blood type was A Rh negative. The second infant required 3 whole blood transfusions during the first six weeks of life. A transfusion of 10 ml. per kilogram of body weight was given when hemoglobin concentration fell to 7 gm. per 100 ml. In the third pregnancy, because of a rising maternal anti-D titer, amniocentesis was performed and interpreted as indicative of moderate to severe intrauterine hemolysis. For this reason labor was induced at thirty-seven weeks gestation.

	Birth order		
	First	*Second*	*Third*
Birth date	7-20-59	6-16-62	10-3-63
Sex-weight (gm.)	F-3,380	F-2,977	F-2,920
Blood type		Rh positive	Rh positive
Direct Coombs		Positive	Positive
Jaundice	None	Slight	None
Peak total bilirubin (mg.%)		9.3 (2 d)	6.0 (2 d)
Hemoglobin (gm.%)		17.1 (1 d)	12.2 (cord)
		12.6 (2 d)	13.8 (2 d)
		7.0 (12 d)	6.0 (10 d)
		* (14 d)	* (10 d)
		11.5 (16 d)	10.3 (10 d)
			7.5 (17 d)
			* (17 d)
		2 subsequent whole blood transfusions over next 28 days	11.2 (17 d)
			8.5 (26 d)
			10.7 (85 d)
			12.0 (93 d)

*Indicates whole blood transfusion

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	Birth order				
	First	*Second*	*Fourth*	*Fifth*	*Sixth*
Birth date	3-6-58	2-1-59	9-4-60	1-6-62	1-6-64
Sex-weight (gm.)	F-3,686	M-4,111	F-3,600	F-3,657	F-3,742
Blood type	Rh positive	Rh positive	Rh positive	Rh positive	Rh negative
Direct Coombs	Negative	Positive	Positive	Positive	Negative
Jaundice	None	None	None	None	None
Peak total bilirubin (mg.%)		2.5	3.5	5.5	
Hemoglobin (gm.%)		17.0 (cord)	14.9 (cord)	15.8 (cord)	
		13.4 (2 d)	11.0 (5 d)	7.0 (17 d)	
		12.6 (4 d)	6.8 (21 d)	* (17 d)	
			* (22 d)	12.9 (18 d)	
			10.9 (22 d)	8.2 (25 d)	
			10.0 (29 d)	9.0 (32 d)	
			>10.0 (35 d)	>10.0 (42 d)	

*Indicates whole blood transfusion

Family 2. The maternal blood type was B Rh negative. The third pregnancy resulted in an early spontaneous abortion. Both the fourth and fifth infants were transfused with whole blood, 10 ml. per kilogram of body weight.

DISCUSSION

Before discovery of the Rh system, congenital anemia of the newborn was the designation for an unclassified group of anemias that could not be attributed to such conditions as hemorrhagic disease of the newborn, traumatic and spontaneous hemorrhage, tuberculosis, syphilis, pyogenic infection, icterus gravis, hemolytic icterus, diphtheria, and malaria. More than forty years ago Holt and Howland[4] stated that "anemia sometimes occurs in the first two or three months of life in a severe form without any discoverable cause." In 1930, Gelston and Sappington[5] pointed out that those infants destined to have anemia due to antenatal causes usually had normal hemoglobin and erythrocyte values at the time of birth and did not develop severe anemia until after ten days.

Abt's[6] description of congenital anemia of the newborn is well suited to the clinical course of the erythroblastotic infant with an unusual ability to conjugate bilirubin. "The infants are born of healthy parents, in normal spontaneous labor, and from their history has been excluded all evidence of birth injury, hemorrhage, hemorrhagic disease, infection, and prenatal poisoning. Within the first two weeks of life, while thriving and behaving in every way as normal infants, they become extremely pale. This pallor is a sheet-like whiteness; in several cases it was reported by the nurse, attendant, or mother that the infant was as pale as the white bed sheets. The infants nurse well, are afebrile, have normal periods of sleep and wakefulness, cry lustily and vigorously, and aside from the marked and startling pallor, show no signs of ill being."

In 1931, Pasachoff and Wilson[7] reviewed the world literature on congenital anemia of the newborn. They described 14 cases and mentioned an additional 14 infants. The only constant and characteristic clinical sign was pallor, usually first noted several days after birth. Mild icterus was noted early in only 4 babies. The spleen was palpable in 7 of the 14 children described. All but 2 made complete recoveries, some with benefit of whole blood transfusion which appeared to shorten recovery time. They believed that this condition occurs more frequently than the few case reports would indicate and that pallor in the first weeks of life should be investigated.

Segar and Stoeffler,[8] in 1932, reported a family in which anemia of the newborn occurred in 3 successive siblings. The mother first delivered a stillborn infant and then 3 successive pregnancies resulted in 3 infants who developed marked pallor between the fourth and tenth days after birth. No mention of icterus was made. All of these infants required repeated whole blood transfusions until concentrations of hemoglobin rose spontaneously between the fourth and eleventh weeks. This report strongly suggests that the anemia in these infants was due to erythroblastosis.

Definition is now possible for many of the anemias which were previously grouped together in the syndrome called congenital anemia of the newborn. Posthemorrhagic anemia and shock in the newborn was reviewed, classified, and described by Kirkman and Riley[9] who found 1 case of posthemorrhagic anemia for every 5

cases of erythroblastosis. Careful examination of the placenta and its membranes and cord for evidence of rupture, tear, and congenital anomaly should be done at every delivery. Fetal-maternal transfusion has recently been described as a cause of anemia in the newborn.[10,11] To these congenital anemias which are not usually accompanied by jaundice may be added anicteric erythroblastosis.

The clinical manifestations of erythroblastosis will vary from one infant to another depending on the extent of hemolysis, mild, moderate, or severe (hydrops fetalis). The major features of the disease, anemia and jaundice, combine, each with an independent spectrum of severity, to account for the variations in clinical manifestations. These manifestations in the infant with erythroblastosis appear to depend on at least 4 major factors; the rate of red cell production, the rate of red cell destruction, the capacity to conjugate bilirubin, and the ability to excrete the bile pigments formed. With active hemolysis the capacity of the liver to conjugate bilirubin is perhaps the major factor that determines the degree of clinical icterus. The wide variation in this function of the newborn is evident by the different degrees of physiological jaundice observed in any newborn nursery.

Although most newborns acquire the capacity for bilirubin conjugation quite rapidly, the mechanism truly evolves over a period of several weeks. It is only rarely that a newborn appears to have a mature mechanism for bilirubin conjugation at the time of birth.[12] The infant with hemolytic disease of the newborn who does not become jaundiced clinically but is markedly anemic has obviously demonstrated an unusual capacity for bilirubin conjugation. It is recommended that even in the absence of clinical icterus the infant with a potential blood incompatibility, especially with a positive direct Coombs' test, be followed closely for anemia during the first two months of life.

SUMMARY

Infants with erythroblastosis fetalis with anemia but without hyperbilirubinemia have been observed. Earlier reports of congenital anemia of the newborn include descriptions of similar cases. Perhaps emphasis on the importance and hazard of jaundice has caused us to overlook severe anemia as the major problem in certain cases of erythroblastosis. All newborns with a suspected hemolytic anemia should be followed closely for progressive anemia even if they do not exhibit jaundice in the first few days of life.

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Intramural Hematoma of the Duodenum

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INTRAMURAL HEMATOMA of the duodenum was first described by McLachlan[1] in 1838. Since then, a total of 33 cases have been reported in the literature. Moore and Erlandson[2] have recently reviewed the subject. Fifty-three percent of these cases occurred in children 12 years or younger. Since Felson's[3] article in 1954, in which the radiographic features of this entity were reported, the frequency of correct diagnosis before operation has increased. The purpose of this report is to present a case of intramural hematoma of the duodenum, in which the diagnosis was made without surgical exploration and conservative therapy was successful. The clinical and radiographic features of this entity will be emphasized.

CASE REPORT

J.S.P., a 6-year-old Caucasian female, was admitted to the 862nd Medical Group Hospital because of vomiting and abdominal pain. She sustained a blunt injury to the upper abdomen via a bicycle handlebar fifty-two hours before admission. After several minutes, she had no apparent distress. Forty-eight hours before admission, she developed bile-stained emesis. She was seen in the outpatient department thirty-eight hours before admission and was found to have mild tenderness around a superficial 2 × 2 cm. hematoma of the upper portion of the abdominal wall (Fig. 1). Examination of the abdomen was otherwise negative; bowel sounds were present. There were no other abnormalities. Since she did not appear acutely ill, she was allowed to return home. The parents were instructed to apply cold compresses to the hematoma of the abdominal wall. There was no history or physical evidence of trauma to the head. She was seen again in the outpatient department and it was decided she should be hospitalized.

Past history. The patient's general health had been uneventful. There was no familial history of blood dyscrasia.

Physical examination on admission. The patient was a well-developed, well-nourished, Caucasian female. She complained of mild abdominal pain. Pulse was 96, respiration 18, temperature 98, and blood pressure 100/60. There were no signs of trauma to the head. The pupils were round, equal, and reactive to light and accommodation. Funduscopic examination revealed no papilledema, hemorrhages, or exudate. The heart had a regular sinus rhythm and no murmurs. Lung fields were clear to auscultation and percussion. In the abdomen there was a 2 × 2 cm. subcutaneous hematoma to the right of the midline between the xyphoid and the umbilicus. There was moderate involuntary guarding on the left. No masses were palpable. The bowel sounds were active. Rectal examination revealed no abnormal masses or tenderness. Neurological examination revealed an alert, active female. There were no abnormal or localizing neurological findings.

Laboratory data on admission. Laboratory data revealed a hematocrit of 36%, hemoglobin of 12 gm. per 100 ml., and white blood count of 6,100 per centimeter, with 50% neutrophils, 1% bands, 44% lymphocytes, 4% monocytes, and 1% basophils. The platelets were adequate. The initial urine contained 3 to 5 red blood cells per high-power field but was otherwise normal. The microscopic hematuria disappeared on the following day. The bleeding time was two minutes. The Lee White coagulation time was four and one-half minutes. The prothrombin time was 14.5 seconds with a control of 13.5 seconds. The stool and vomitus were negative for blood. The serum amylase was 232 units. An upper gastrointestinal series, obtained the day after admission because of persistent vomiting, demonstrated a normal esophagus and stomach. The first and second portions of the duodenum were dilated and there was delayed emptying from the second to the third portion of the duodenum (Fig. 2). When the third portion of the duodenum filled, it was noted that the lumen was considerably constricted and measured 2 to 3 mm. This portion of the duodenum was considerably flattened out and the mucosa was stretched. The narrowed lumen extended over a length of 3 cm. (Fig. 3). The impression was that these findings indicated an intramural hematoma of the third portion of the duodenum. The chest film taken on admission demonstrated a considerable amount of fluid in the stomach.

Hospital course. During the first seventy-two hours after admission, the patient continued to have profuse vomiting, and parenteral fluids were given. Following this period, she tolerated oral fluids. She had no further emesis after the sixth hospital day. Follow-up hemogram was 11.5 gm. percent, with a hematocrit of 34%. Stool remained negative for blood. On the ninth hospital day the serum amylase was 600 units. A repeat gastrointestinal series at this time demonstrated that the lumen of the third portion of the duodenum had returned to normal size (Fig. 4). There was a minimal delay in emptying from the second into the third portion of the duodenum. There was no evidence of the intramural lesion. The child was discharged from the hospital on the ninth hospital day. She tolerated a regular diet without nausea or vomiting. Since discharge, she has been observed periodically and has remained asymptomatic.

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Fig. 1. The circled area demonstrates the site of the superficial hematoma of the abdominal wall.



Fig. 2. Roentgenogram of initial upper gastrointestinal series, which demonstrates the dilatation of the third portion of the duodenum



Fig. 3. Roentgenogram of the initial gastrointestinal series, which demonstrates the compromise of the distal third portion of the duodenum. The "coiled spring appearance" of the mucosa is shown.

DISCUSSION

Intramural hematoma of the duodenum is a distinct clinical entity; however, it is likely that many cases have not been recognized. Hematoma throughout various portions of the intestine have been described, and in 50% of these cases, the site of involvement has been in the duodenum.[4] The reason for this high incidence in the duodenum probably is due to the fact that the duodenum is relatively immobile, being bound by the head of the pancreas and held in position by the pancreatic and common bile ducts and, distally, by the ligament of Treitz.[5] It is because of this fixed position and the relationship of the duodenum to the vertebral column that blunt trauma can produce an intramural hematoma. Trauma shears the small vessels along the mesentery, and a clot forms between the serosal and muscularis layers of the bowel.[4] Blood dyscrasias,[6] pancreatic tumors, and anticoagulant therapy[7] have also been reported as etiologic factors.

The diagnosis should be considered whenever there is a history of abdominal trauma, however trivial it may seem. In children, the history of trauma may not be obtained. This is frequently followed by an asymptomatic period of one to two days, after which the symptoms of a high, small-bowel obstruction predominate. There is periumbilical pain and persistent vomiting. A palpable epigastric mass may or may not be found.[8] It may be difficult to differentiate pancreatitis from this entity, due to the associated trauma to the pancreas.[2]

The radiographic findings as found in the



Fig. 4. A follow-up upper gastrointestinal series done six days after the initial study shows that the third portion of the duodenum is now within normal limits.

gastrointestinal series are diagnostic.[3] The typical picture is that of a sharply marginated mass, which partially or completely encroaches upon the lumen of the duodenum, usually at its third portion. The valvulae conniventes are stretched and crowded together, producing a "coiled spring appearance." There may be extrinsic pressure on the greater curvature of the antrum of the stomach or on a portion of the transverse colon, depending upon the size of the mass.

Most of the cases reported thus far have been treated surgically.[2] The surgical procedure has varied from simple drainage of the hematoma to gastrojejunostomy or cholecystojejunostomy.[4] It has also been stated that with nonoperative therapy, complications such as adhesions, infection, or hemoperitoneum may occur.[4] On the other hand, Felson and Levin reported on 4 cases in which nonoperative treatment was successful in 3. The present case is another instance of successful therapy based on nonoperative management. In one week, the hematoma completely reabsorbed and a follow-up examination in six weeks revealed no evidence of any late complications.

SUMMARY

Intramural hematoma of the duodenum occurs most frequently in children and is usually caused by trauma. There is a latent period before onset of symptoms of high intestinal obstruction. The radiographic findings are described and consist of stretched valvulae conniventes, signifying an intramural mass. A patient is presented who was successfully managed without operation.

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Cardiovascular Aspects of the Collagen Diseases

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THE NUMBER OF syndromes that are grouped under the term "collagen disease" is lengthy and not always agreed on by all authorities. The term, first suggested by Klemperer in 1941,[1] was immediately popular and since then somewhat over used. Klemperer[2] has subsequently pointed out that while the histopathologic changes are similar, and to some extent involve a common anatomic structure, the various diseases are not identical or even necessarily related. The term "collagen diseases" has not met with unqualified approval, and Venters and Good[3] have suggested that while "connective tissue diseases" is better than "collagen diseases" "mesenchymal diseases" is probably even better.

In the table are listed the diseases, or rather syndromes, included. The list is lengthy and perhaps somewhat repetitious. Several are probably variations of polyarteritis, as suggested by Zeek.[4]

The etiology of collagen diseases is not definitely known, but the current concept is that they share in common a hypersensitivity or immunologic background. Klinge in 1933[5] observed that the changes noted in rheumatic fever involved alteration of the connective tissues and pointed out the similarity between this pathological picture and the changes seen with serum sickness and periarteritis. Fibrinoid degeneration of the connective tissue is present to some degree in all of these diseases, as it is in allergic tissue reactions, and, thus, it was postulated that the collagen diseases have an allergic basis. Since that time, many observations support this concept, and current ideas on pathogenesis have been summarized recently.[3]

The characteristic pathological finding is that of changes in the connective tissue with swelling and hyalinization, designated as "fibrinoid swelling" by Klinge.[5] This term was coined to postulate that the hyaline-like material seen represented fibrin, but as has been subsequently demonstrated, this is not necessarily fibrin.[6] In addition, in the various diseases there are varying degrees of inflammatory changes with necrosis, granulomatous and proliferative lesions, and fibrosis, particularly of the vascular structures. The varying clinical profiles of these diseases depend on the distribution of the involved areas and, also, on which of the listed pathological changes predominate. The kidneys seem to be particularly susceptible to involvement in these diseases, with renal involvement occurring in most. Renal disease is associated with the vascular changes as in other areas but, importantly, with specific involvement of the glomeruli, not as a part of the generalized vascular disease. Adequate renal function is vital, and with the kidney's role in hypertension, renal involvement frequently becomes the most important aspect of the disease.[7]

Clinically, the connective tissue diseases exhibit widely different profiles but share certain similarities. Characteristically, multiple system involvement is noted, and while in typical cases the patterns are clear, in atypical cases they shade one into another, and frequently an accurate classification cannot be made. As noted previously, renal involvement is common, evidenced by abnormalities in the urinalysis and other parameters of renal function varying from mild to severe, with azotemia and death due to renal failure not uncommon. Hypertension occurs quite commonly and is presumably mediated through the rennin-angiotensin mechanism but it can also be a function of widespread arterial disease with actual decrease in the available vascular bed.

Cardiac involvement is also quite common, on the basis of disease of the coronary arteries, the alterations of cardiac connective tissue not including the vascular bed but including the valvular structures, the common finding of systemic hypertension, and, not uncommonly, the elevation of the pulmonary vascular resistance.[8] The mesenchymal diseases also have in common a lack of response to specific therapy, but in

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general, therapy with steroids is usually recommended with varying clinical response. The use of steroids in these diseases has been implicated in the pathogenesis of the vascular involvement noted.[9]

We will discuss the clinical aspects of cardiovascular involvement of these diseases in the order that they appear, with no implication in the order. Comment will be made as to involvement in the pediatric age group.

SYSTEMIC LUPUS ERYTHEMATOSUS

In general, this is more or less the prototype of this group of diseases and presents with protean manifestations. There is a great deal of evidence both clinically and from the laboratory implicating immunologic mechanisms in its pathogenesis[3] The exact incidence of the disease is unknown but is apparently increasing, though this is probably at least partly due to improved diagnostic methods and a greater awareness of the possibility. It is a not uncommon disease in the pediatric age group,[10] usually beginning during the second decade, though it has been reported to be present at birth. The disease in children has a tendency to be a more rapidly progressive disease than in adults. There is a sex-linked incidence, the disease being far more common in females than in males, both in the pediatric and adult groups. The tendency toward females and the higher incidence during adolescence suggests a hormonal relationship, though this relationship is not clear. The association of this disease with exposure to sunlight, history of infection, and familial occurrence would be listed under predisposing factors, though their importance is not well elucidated. The immunologic aspects of this disease are multiple and not germane to this discussion, other than to mention that a decrease in the serum protein with an increase in the globulin fraction, a high incidence in false-positive serologic tests for syphilis, and the presence of antinuclear gamma globulin factors occur in this disease. The lupus erythematosus cell phenomena are related to the latter and are the sine qua non of this disease. This is mediated by a gamma globulin that exists in the serums of these patients which reacts with damaged cell nuclei, producing extrusion from the cell and phagocytosis by polymorphonuclear cells. Whether the lupus erythematosus phenomenon is involved in the pathogenesis of this disease is not known.

As mentioned, the manifestations of this disease are widespread, involving multiple systems, predominantly, though apparently not entirely, due to vascular involvement, this being the most consistent and widespread pathological finding. Capillary involvement is prominent with widespread involvement of the small arteries, though involvement of the larger arteries occurs as well. These changes are those of hyaline fibrinoid necrosis of the media, associated with proliferation and swelling of the intima, and perivascular inflammation. This process may involve large vessels, even as large as the aorta, with thrombosis and infarction distally.[7] Renal arterial involvement occurs and a characteristic glomerular lesion is noted. An abnormal urinalysis is almost always found in children.[10] Lupus nephritis is the most serious manifestation of the disease, and while early renal involvement in adults is not as common as in children, it is the most frequent cause of death in all age groups. Hypertension and renal failure are associated with renal involvement. Pulmonary involvement occurs, with an interstitial pneumonia seen. Cardiac involvement is common, occurring in approximately 50% of the patients. Pericarditis is frequent and may be a presenting finding of the disease; it has been reported to occur before the onset of other manifestations. Libman-Sacks valvular endocarditis occurs with significant systolic and diastolic murmurs. Cardiac enlargement with gallop rhythm and systolic murmurs not associated with definite valvular disease but with myocarditis is commonly seen and frequently contributes to the demise of these patients.

Treatment involves hospitalization during diagnostic studies and initiation of therapy.[10] Anemia is common but transfusion is difficult due to a cross-matching problem, and infections should be managed as usual. Steroid therapy has been demonstrated as beneficial, with dramatic improvement of most of the manifestations of the disease, though with lupus nephritis results have not been consistently good.[11] The complications and precautions associated with steroid therapy are well known and will not be commented on other than to mention that their use has been implicated as a possible factor in worsening the vasculitis.[12]

Finally, a brief comment should be made in regard to drug-induced lupus. Drugs reported to cause the clinical and laboratory picture of lupus include most commonly hydralazine; several of the anticonvulsants, such as trimethadione (Tridione®), diphenylhydantoin (Dilantin®), and paramethadione (Paradione®); sulfa drugs, such as sulfamethoxypyridazine (Kynex®); and penicillin.[10] Death has resulted in such cases but, more importantly, apparent cure has been noted following cessation of drug administration. In the

SYNDROMES INCLUDED
IN THE CONNECTIVE TISSUE DISEASES

1. Disseminated lupus erythematosus
2. Rheumatoid arthritis
3. Rheumatic fever
4. Dermatomyositis
5. Scleroderma
6. Thrombotic thrombocytopenic purpura
7. Henoch-Schoenlein purpura
8. Goodpasture's syndrome
9. Sjögren-Mikulicz syndrome
10. Polyarteritis nodosa*
    - A. Classic: Kussmaul-Maier type
    - B. Hypersensitivity angiitis
    - C. Rheumatic arteritis
    - D. Allergic granulomatous angiitis
    - E. Temporal arteritis
    - F. Miscellaneous group

*Classification as proposed by Zeek

majority of cases, however, no such factor has been implicated.

RHEUMATOID ARTHRITIS

A discussion as to whether or not Still's disease and rheumatoid arthritis, as more typically seen in adults, are the same disease is not germane here. Rheumatoid arthritis is a disease of the viscera as well as the joints, muscles, and skin.[7] Definite cardiovascular involvement is not commonly reported in children, though the overall incidence of cardiac involvement has been reported as from 10 to 50%.[8] The age of onset of rheumatoid arthritis in children has a peak at age 5 years and is more commonly noted in girls; this incidence as to sex is noted in adults as well. The etiology is not known, though hereditary and immunologic factors seem to be important. Serologic abnormalities in this disease have been noted and the volume of literature on this aspect is overwhelming. The "rheumatoid factors" are apparently gamma globulins and are present in 60 to 80% of adults but in only 20 to 40% of children. Modifications of these techniques have been reported to show a higher incidence of positives in children, comparable to that found in adults. The place of these serologic factors in pathogenesis of the disease is not known.

Widespread involvement is not as common in children as in adults, though it does occur. The incidence of amyloidosis associated with rheumatoid arthritis makes it somewhat difficult to determine the degree of specific rheumatic cardiovascular involvement, since amyloidosis per se has cardiac manifestations. A nonspecific glomerulitis has been reported with rheumatoid arthritis. Vascular lesions have been observed in the skin, muscles, peripheral nerves, and viscera and, particularly, in the heart, gastrointestinal tract, and kidneys. Steroid therapy has been implicated in the pathogenesis of these lesions.[12] Cardiac involvement is not common in children but, if present, usually is that of pericarditis. Aortic involvement with aortic insufficiency has been reported in children, and both aortic and mitral involvement is reported in adults, particularly with spondylitis. It is important to note that it can be very difficult to differentiate absolutely the collagen diseases, particularly rheumatoid arthritis, rheumatic fever, lupus, and polyarteritis and, hence, cardiac involvement may be associated with another disease rather than as part of rheumatoid arthritis.

RHEUMATIC FEVER

This is a disease in which the acute form is predominantly a pediatric problem, though the late sequelae are adult problems. It is an inflammatory disease, predominantly involving connective tissue. Cardiac involvement is of paramount importance, since all other manifestations are transient and without important sequelae. Group A, beta-hemolytic streptococcal infections are operative in the etiology of the disease, though the exact role in pathogenesis is not known. A familial tendency is noted, the data suggesting that susceptibility is as an autosomal recessive characteristic.[13] An immunologic mechanism is thought to be operating, but efforts to elucidate this have not been definitely successful. Serologically, these patients cannot be clearly differentiated from the normal, though the antibody responses to streptococcal antigens, most commonly the O antigen, are exaggerated. It has been shown that antigens occurring in heart muscle cross react with streptococcal antigens; however, the significance of these observations in the pathogenesis is not known.[14] There is no specific diagnostic test available, the diagnosis remaining strictly a clinical problem. Vascular involvement does occur in severe cases, though it is uncommon and no permanent residue is noted.

Cardiac involvement is common with generalized carditis involving the pericardium, myocardium, and endocardium, the pathognomic lesion being the Aschoff body. The clinical manifestations of this disease are best summarized in the modified Jones criteria and will not be commented on.

As mentioned initially, the long-term sequelae of rheumatic fever are confined to the heart and in essence consist of scarring, with distortion of the valvular structures. This process involves most commonly the valves on the left side,

though right-sided involvement does occur. It is important to note that rheumatic fever is a disease associated with streptococcal infection and hence is preventable.[3]

The value of steroids in the treatment of this disease is controversial, though all agree that in the severe fulminating picture steroids may be lifesaving.[15] As to whether or not they alter the long-term picture is not clear at this time. The association of the disease with streptococcal infection, however, is such that prophylaxis against recurrent infection is indicated certainly in children and young adults, probably indefinitely. It is of interest to note that the clinical profile of rheumatic fever is changing. This is not necessarily related to present methods of treatment, the changes being noted before the use of steroids or effective prophylaxis, at least in this country.

DERMATOMYOSITIS

This is a disease characterized by inflammatory changes involving particularly the skin and striated musculature.[16] That systemic involvement occurs has been noted, though not as commonly as in the other syndromes discussed. It occurs commonly in the pediatric age group, approximately one-third of the reported cases being in children. There is a sex-related predilection, the disease appearing in females approximately twice as often as in males. As in the other collagen diseases, a multiplicity of etiologic factors has been implicated on rather flimsy grounds. Hypersensitivity probably plays some part, though the relationship is not as definite as in other members of the group. The frequent association of the disease with malignant lesions in the adult is well known but apparently only coincidental in children. Serologic abnormalities are not common in dermatomyositis, though increase in gamma globulin and the presence of rheumatoid factor have been demonstrated. Again, it should be emphasized that it is frequently difficult to clearly differentiate these diseases.

Vascular involvement occurs and is apparently causally related to the clinical findings, being reported in the skin, muscles, mucosa, and kidneys. The relative lack of vascular involvement has been thought to be a major diagnostic criteria for dermatomyositis, but the value of these criteria is uncertain now. It may be relevant that cardiac involvement has been associated with the use of steroids. Clinical evidence of cardiovascular disease is rare, but pericarditis and electrocardiographic changes suggestive of myocardial involvement have been reported. Clinically, renal disease is said to be rare, though renal biopsy has been reported to reveal histological changes even in the absence of clinical evidence of renal disease. Raynaud's phenomenon is a not uncommon complication of the disease.

Reports as to the prognosis vary, though it is estimated that approximately 50% will die. Prognosis in children does not differ markedly from adults, the data suggesting that about one-third succumb and one-third are crippled, while the remaining one-third recover completely. The clinical pattern of the disease does not furnish reliable clues as to the prognosis, though cardiac and palatorespiratory involvement are in general poor prognostic signs.

Drug therapy has been disappointing, the mainstay of treatment being adequate nursing care and physiotherapy. Steroids may give striking symptomatic improvement in the acute phase of the disease but do not alter the long-term prognosis.

SCLERODERMA

Scleroderma is a disease primarily involving the skin but frequently presenting widespread visceral lesions as well,[17] and the term "progressive systemic sclerosis" has been suggested as a more inclusive term. The characteristic lesion is that of atrophy of the epidermis and its appendages. Fibrosis of the collagenous subcutaneous tissue follows with areas of contraction and deformity. Vascular involvement occurs, both venous and arterial, but is apparently not frequently found. It is of interest to note that the presence of fibrinogen in the renal lesions has been determined immunohistochemically, in contrast to the gamma globulin frequently demonstrated in the other diseases.[3] Serologic changes are reported and include hypergammaglobulinemia, presence of antinuclear activity, and, occasionally, demonstration of the lupus erythematosus phenomenon and rheumatoid factor. These findings suggest the presence of an immunologic factor in this disease, though pathogenesis remains obscure.

Clinically, vascular involvement is suggested by the frequent presence of Raynaud's phenomenon, renal abnormalities, noted clinically by the presence of abnormal renal function studies or renal failure, and hypertension.[17] Cardiac involvement is noted clinically by the development of exertional dyspnea, orthopnea, cyanosis, and palpitations. Associated with this are nonspecific electrocardiographic changes, cardiomegaly, arrhythmias, cardiac murmurs (usually systolic), and, at times, the presence of pericarditis. Because of the tendency to involvement of the lungs with fibrotic changes, it is difficult to differentiate clinically cardiac involvement from that

due to the pulmonary changes. Changes in the gastrointestinal tract are an important part of this disease, particularly the atonic and fibrotic changes noted in the esophagus with dysphagia and regurgitation.

There is no satisfactory drug treatment for the disease. Prognosis is difficult to determine due to the marked variation in the clinical course. It is poor in those with rapid progression and in those with cardiac involvement and uniformly fatal in those with renal involvement.

THROMBOTIC THROMBOCYTOPENIC PURPURA

This is a diffuse vascular disease, characterized clinically by thrombocytopenic purpura, hemolytic anemia, and neurological abnormalities.[7] It is usually an acute and rapidly fatal disease, though it may run a protracted course, has an approximately equal sex distribution, and has been reported in all ages. Pathologically, widespread vascular lesions are present with many hyaline thrombi involving the small arteries, arterioles, and arteriolar capillary junctions. Inflammatory changes are not part of the picture. These findings have been noted in all organs but predominantly in the heart, kidneys, brain, adrenals, and the pancreas. Symptomatology is thus widely variable. An allergic or hypersensitivity reaction is suspected as an etiologic mechanism. Fibrin has been localized in the lesions but no reaction was observed with rabbit antihuman platelet antibodies. Thus, the thrombotic lesions are probably not due to platelet thrombi, thrombocytopenia is not secondary to platelet utilization, and the vascular lesions represent a primary vascular injury.

The cardiac manifestations include tachycardia, murmurs of various descriptions (usually systolic), and cardiomegaly. These findings could well be due to the anemia associated with the disease; however, the coronary vessels are involved, and areas of thrombosis and infarction are noted in the myocardium at necropsy.

Except rarely, treatment has been of little value, though early vigorous treatment with high steroid dosages have been reported to produce prolonged remissions when combined with splenectomy.

HENOCH-SCHOENLEIN PURPURA

Anaphylactoid purpura is characterized by nonthrombopenic purpura, most prominent over the lower trunk and legs, crises of abdominal pain associated with melena, arthralgia, and urinary findings resembling acute nephritis.[19] Etiology is unknown, though available data suggest a hypersensitivity background. Sex incidence reveals a slight male predominance. There is a peak incidence between the fourth and fifth year in children, though it has been reported as early as 6 months of age. An allergic history in the involved patient is approximately twice that of the general population, and a history of a preceding respiratory infection can be elicited in approximately two-thirds and is presumably related. Serologic abnormalities have not been demonstrated, eosinophilia is common, and in adults progression into polyarteritis has been reported. Pathologically, the disease is an acute vasculitis, and the symptoms are dependent on the vessels involved. Renal changes are those of glomerular involvement with few significant arterial changes. Gastrointestinal hemorrhage can be life threatening, though death is usually associated with the development of chronic renal disease, renal failure, and hypertension. Cardiac involvement is in general not a part of the syndrome in the absence of chronic renal disease with hypertension.

Treatment involves a search for and treatment of a possible infective or allergic agent. Antihistamines are of little value. Steroids have been beneficial, particularly early in the course of the disease, but have been of little value in treating those with severe renal disease.

GOODPASTURE'S SYNDROME

This is a syndrome characterized by pulmonary hemorrhage or hemorrhagic pneumonia and glomerulonephritis.[7] Primarily, the disease affects previously healthy young males and is fatal within a period of several months to one year. Clinically, it occurs in two phases: initially, the pulmonary phase with hemoptysis, dyspnea, and chest pain followed by insidious development of renal disease with proteinuria, microscopic hematuria, and granular and hyaline casts. Nitrogen retention occurs and is progressive, and death usually results from renal failure though the pulmonary disease is occasionally fatal. Hypertension is rarely seen. Involvement of other organ systems is rare.

The etiology is obscure, but a hypersensitivity mechanism is hypothesized and the presence of gamma globulin has been noted in the vascular lesions. Treatment with steroids in high dosages has been reported to be of benefit if given early in the disease but is of no value in those with well-established renal involvement.

SJÖGREN-MIKULICZ SYNDROME

This syndrome is characterized by dryness of the eyes and all mucous membranes, hyposecretion of the exocrine glands, parotid swelling, and sys-

temic manifestations. A relationship with the connective tissue diseases is noted, the syndrome being reported with rheumatoid arthritis, polymyositis, and scleroderma. The association with other collagen diseases may be the background of the vascular changes noted.

POLYARTERITIS

Polyarteritis is a progressive, necrotizing, inflammatory disease of the medium and small-sized muscular arteries and is the arch type of the vascular involvement in the collagen diseases. The vascular lesions vary in the size of the vessels involved, area affected, degree of thrombosis, character of the inflammatory infiltrate, and degree of necrosis.[20] Thus, the clinical picture varies widely. No age group is immune, and the classical disease is noted more often in males. The widespread vascular lesions are associated with a variety of signs and symptoms including arthritis, myalgia, fever, gastrointestinal symptoms, peripheral and central nervous system damage, and cardiac and renal involvement. Leukocytosis with eosinophilia and an elevated sedimentation rate are noted.

Cardiac involvement is not uncommon, being noted pathologically in approximately 50%. Clinically, this is manifest by cardiomegaly, tachycardia, congestive heart failure, and occasionally electrocardiographic changes. Angina is uncommon, however, necropsy frequently shows small areas of infarction, and death has been reported from myocardial infarction.[20] In cases reported occurring during infancy, cardiac involvement is extensive, the majority evidencing progressive heart failure or sudden death.[19] Necrosis of the vessel walls with thrombus formation is noted; occasionally, rupture may occur with resulting brisk hemorrhage and, on occasion, death. The kidney is the most common organ involved, occurring in 70 to 100% of the reported cases.[7] Hypertension occurs in 50% of the reported cases, usually on a renal basis, though widespread fibrosis with resulting constriction of the vascular bed may contribute to this. The presence or absence of pulmonary involvement shows an interesting variation by sex; in those with pulmonary involvement, the male predominance is not present. Granulomatous lesions occur and their presence is apparently a variation of the same disease, as noted by Zeek. Hypersensitivity angiitis is considered a variation of polyarteritis but is clinically a more acute and fulminating process.

Hypersensitivity is thought to be involved in the etiology of polyarteritis and its variants. Immunologic studies have revealed the presence of gamma globulin in the vascular lesions; hypergammaglobulinemia is noted, and there is morphological similarity between the polyarteritic vascular lesions and lesions associated with experimental serum sickness in animals.[3]

Drug therapy is disappointing, but steroids have been reported to be of benefit, though their use has not been shown to alter the long-term prognosis. Comparison of treated and untreated cases at the end of one year definitely favors the treated cases, but by the third and fourth year, this advantage is largely gone.

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Clinical Evaluation of Noisy Respiration in Infancy

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THE PROBLEM OF noisy respiration in the first two years of life is frequent. Noisy breathing in infancy may be produced by nearly all forms of obstruction of the respiratory tract recognized in later life, as well as a number of specific entities found only during infancy. Accurate clinical evaluation is invariably important. Determination of the site of the noise as well as its etiology is essential for rational management.

PHYSICS OF NOISY RESPIRATION

Normally inspiration and expiration require approximately equal periods of time. The pause following expiration, usually termed the expiratory pause, is not considered a part of expiration (Fig. 1).[1]

Normally, inspiration and expiration occur at intrapulmonic pressure of 2 to 3 mm. Hg below and above atmospheric pressure, respectively (Fig. 2).

In the presence of airway obstruction, marked changes occur in the relative length of time required for each phase of respiration and in the intrapulmonic pressures associated with inspiration and expiration.[2] These changes in pressure may reach magnitudes of 30 to 80 mm. Hg below atmospheric pressure during inspiration and may reach 60 to 100 mm. Hg above atmospheric pressure during expiration. These changes in intrapulmonic pressure produce striking changes in the physical signs of respiration. These changes are particularly marked in the relatively flexible thoracic cage of the infant.

Noisy respiration is almost always due to some form of airway obstruction. This obstruction must be incomplete, so that sufficient air gets past the obstruction to produce vibrations in the air column of the respiratory tract. Obstruction from any point between the anterior nares and the smallest bronchioles may produce significant respiratory noise. The intensity and the frequency of the noise depend on the diameter of the narrowed aperture, the velocity of the airflow, and the pressure produced proximal to the obstruction relative to the pressure distal to the obstruction. As the aperture decreases in size, the pitch of the noise increases and may be of a whistling or wheezing quality. Increasing the velocity of airflow which is a function of aperture size and relative pressure proximal and distal to the aperture tends to increase the intensity of the noise.

The phase of respiration in which the noise occurs depends primarily on the location of the obstruction. In the lower respiratory tract where dilation of the airway occurs during inspiration and contraction of the airway occurs during expiration, partial obstruction will tend to produce noise more prominently during expiration. As the diameter of the airway decreases during expiration, the factors of aperture size, velocity of flow, and pressure differential become more marked. On the other hand, the upper portions of the respiratory tract do not vary in size with the phases of respiration. The diameter of these airways are fixed by virtue of their cartilaginous and bony skeletons. Partial obstruction in the upper airways tends to produce inspiratory noise. The relative negative pressure in the airway during inspiration tends to pull soft tissue toward the center of the lumen, thereby increasing the degree of obstruction. Expiration with its relative positive pressure tends to push aside obstructing soft tissue. Expiration occurs with ease even in the face of severe upper respiratory inspiratory obstruction.

Likewise, the relative length of the phases of respiration depends primarily on the location of the obstruction for the same reasons outlined above. The relative length of inspiration tends to be greater in upper respiratory obstruction,

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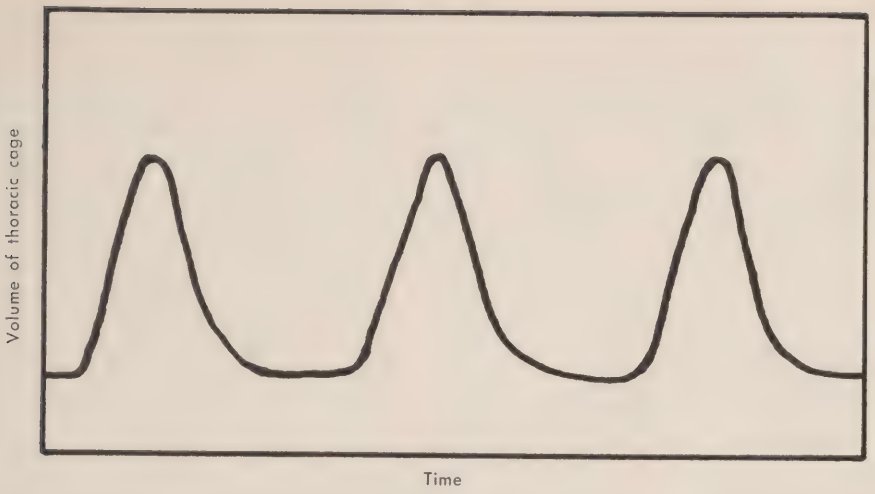


Fig. 1. Curve of normal respiratory movements. Upstroke is inspiration, and downstroke is expiration. There is a pause in respiration at the end of expiration.

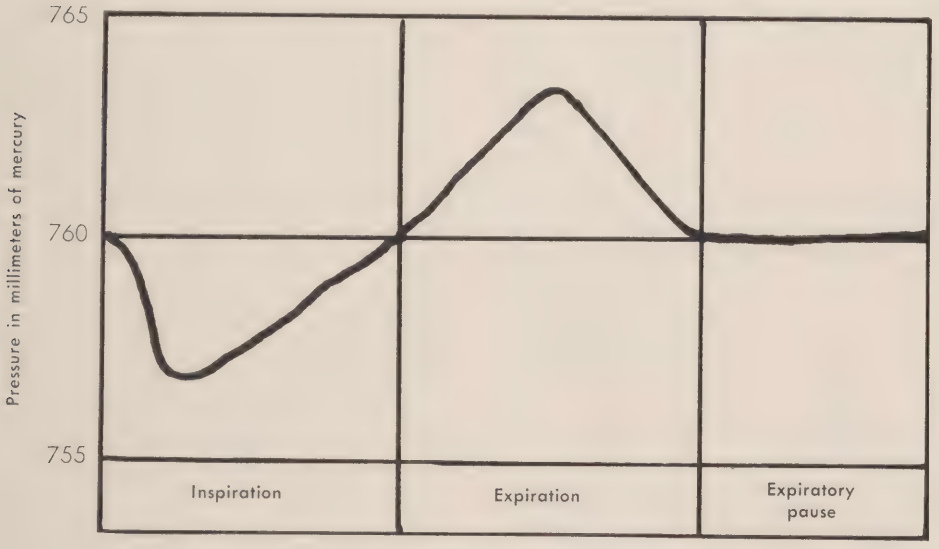


Fig. 2. Curve of intrapulmonic pressure during normal respiration

and the relative length of expiration tends to be greater in lower respiratory obstruction.

PATHOLOGIC STATES

It is helpful in evaluating these clinical problems to differentiate between those present at birth and those which appear later during the first two years of life.

Among the well-recognized causes of upper respiratory obstruction encountered in the immediate neonatal period are bilateral choanal atresia; the Pierre Robin syndrome of cleft palate, hypoplasia of the mandible, and a relatively large tongue; bilateral vocal cord paralysis; subluxation of the arytenoids due to traumatic delivery;[3] laryngomalacia or the exaggerated infantile larynx; stenosis and atresia of the larynx or web of the larynx; papillomas of the larynx; subglottic hemangioma; intrinsic tracheal lesions such as tracheomalacia, absence of tracheal rings, and tracheal stenosis; and extrinsic tracheal compression including tumors of the thyroid, thymus, esophagus, mediastinum, and the vascular rings. Newborns with tracheoesophageal fistulas certainly have noisy respiration due to aspiration but no true airway obstruction. Tetany of the newborn with laryngospasm is usually recognized by the other characteristics of this condition.

Later in infancy, respiratory obstruction may be due to retropharyngeal abscess, adenoid and tonsillar hypertrophy, trauma to the larynx, bilateral abductor paralysis of the vocal cords secondary to the Arnold-Chiari malformation and myasthenia gravis, foreign bodies, laryngeal

diphtheria, laryngotracheobronchitis, respiratory burns, endobronchial granulomas, and neoplasms and cysts of the mediastinum.[4,5] Laryngeal papillomas and subglottic hemangiomas usually make their appearance in the first year of life, although they may be present at birth. Certainly, slowly progressive stridor in an infant suggests these two lesions. Although the vascular ring malformations of double aortic arch, right aortic arch with left ligamentum arteriosum, anomalous innominate artery, and anomalous left common carotid artery produce tracheal obstruction, they are more likely to produce symptoms of dysphagia rather than signs of airway obstruction. The onset of symptoms may be at birth or occur only after several months. Many of these vascular rings remain asymptomatic.[6]

DETERMINATION OF SITE OF LESION

These lesions have several signs in common. All are likely to result in increased respiratory rate, tachycardia, suprasternal and intercostal retraction, use of the accessory muscles of respiration, and cyanosis.[7] Clinically, there are 7 salient differential points of value in determining the site of the lesion: [1] the phase of respiration in which the stridor occurs, [2] the longer phase of respiration, [3] the presence or absence of hyperextension of the neck, [4] the quality of the voice or cry, [5] the presence or absence of difficulty in feeding, [6] the amount of intercurrent pulmonary infection, and [7] auscultation of the point of maximum intensity.

The phase of respiration in which the stridor occurs is more likely to be inspiratory in upper respiratory obstruction. The stridor is usually expiratory in tracheal and bronchial obstruction. Likewise, inspiration will be more likely to be relatively longer than expiration in upper respiratory obstruction. Expiration is usually relatively longer than inspiration in tracheal and bronchial obstruction.

Hyperextension of the neck will be more likely to be present in supraglottic obstruction and extrinsic tracheal obstruction. This sign is usually present in retropharyngeal abscesses and in vascular rings and tumors compressing the trachea. Hyperextension of the neck is unlikely in laryngeal obstruction.

The quality of the voice tends to be normal in all except laryngeal lesions. In laryngeal lesions, the voice may be normal unless the true cords are involved. For example, abductor paralysis of the vocal cords is associated with a normal cry. Laryngeal papillomas usually produce profound hoarseness. The infant's cry will also be hoarse in acute laryngotracheobronchitis and laryngeal diphtheria.

Difficulty in feeding will be seen in extrinsic lesions of the esophagus and trachea, such as mediastinal tumors and vascular rings. Stridor due to neurological abnormalities resulting from infantile myasthenia gravis, brainstem gliomas, and encephalitis are likely to be associated with difficulty in feeding. A tracheoesophageal fistula will also result in extreme feeding difficulties. Laryngeal obstruction and intrinsic tracheobronchial obstruction are rarely associated with feeding problems.

The presence of recurrent pneumonitis tends to occur more frequently with tracheal and bronchial obstruction and is rare, for example, with laryngomalacia.

Auscultation of the chest and neck is likely to give valuable information as to the site of the obstruction. The signs of obstructive emphysema or atelectasis distal to the obstruction are helpful if present.

Helpful radiographic studies in the illucidation of the cause of stridor of undetermined etiology include lateral neck and posteroanterior and lateral chest roentgenograms. These films are useful in demonstrating a number of causes of stridor. A lateral neck roentgenogram may demonstrate an unsuspected retropharyngeal mass or a hypopharyngeal or esophageal foreign body. The lateral chest film gives a good view of the tracheal air column which may be compressed anteriorly in the vascular rings. Mediastinal masses may be apparent on these films. Evidence of obstructive emphysema or atelectasis may be present on the posteroanterior film. In the case of nonopaque foreign bodies of the tracheobronchial tree, fluoroscopy and inspiratory and expiratory films are of value, in that the mediastinum can be seen to shift away from the side of the obstructed bronchus on expiration.

An iodized oil esophagram is often the best means of demonstrating an esophageal foreign body or compression of the esophagus by mediastinal cysts and tumors and vascular rings.

Definitive demonstration of the site and the lesion may require laryngoscopy, tracheoscopy, and bronchoscopy. Tracheography and bronchography yield valuable information in extrinsic as well as intrinsic obstruction of the tracheobronchial tree. If the endoscopist is well prepared with the information obtained from lateral neck and posteroanterior and lateral chest roentgenograms and fluoroscopy of the chest, including an esophagram, he will be in the best position to interpret the abnormalities he may encounter.

Parenthetically, it should be emphasized that the abnormalities under discussion are slight variations from the normal. Gross variations from the normal are not compatible with life. General anesthesia is preferred for these examinations so that the patient is relaxed. Accurate observations of these slight variations from the normal can then be made. The specular examination of the respiratory tract can be followed advantageously by tracheography and bronchography under the same anesthesia.[8]

COMMENTS ON MANAGEMENT

The significant fact is that all of these causes of respiratory obstruction lend themselves to rational management. All of these infants are potentially salvageable. Many of the conditions are self limited, and if the infant can be successfully managed through the first few weeks or months of life, the problem is solved.

An excellent example of this situation is bilateral choanal atresia. This condition should be considered when a newborn fails to ventilate in the presence of respiratory movements (primary hyperpnea).[9] The immediate solution of inserting an oral airway is lifesaving. The newborn is an obligatory nasal breather and only with experience acquires mouth breathing. Fortunately, crying with its attendant mouth breathing often allows these newborns some ventilatory exchange. After a few weeks, the infant is capable of mouth breathing and the danger abates. The nursing care during this period must be extremely careful. Some advocate early operation with the insertion of polyethylene tubes through a perforation of the atretic area. Most of these operations have no hope for permanent improvement, and a much better repair can be done at 4 to 5 years of age. With careful nursing supervision of the oral airway, a tracheotomy can be avoided in the neonatal period. The diagnosis can be made by the inability to pass a fine, soft catheter into the pharynx from the nose. The diagnosis can also be confirmed by the instillation of radiopaque oil into the nasal cavity and by taking a roentgenogram of the lateral view of the nasopharynx in the supine position. If choanal atresia is present, the dye will pool in the posterior portions of the nasal cavities and will not enter the nasopharynx.

The Pierre Robin syndrome is also a mechanical problem which is amenable to careful nursing care. The prolapse of the relatively large tongue into the oropharynx can be handled by pulling the tongue forward with a suture temporarily. Tracheotomy may be necessary, but usually with good nursing supervision of the airway it can be avoided. As the infant grows older, he is able to manage this relatively large tongue successfully and the danger abates.

If neither of these problems exists in a newborn who is making respiratory movements (primary hyperpnea) but inadequately exchanging air, the larynx should be exposed in the delivery room with a Jackson infant laryngoscope. Exposure of the vocal cords will relieve the obstruction of an exaggerated infantile larynx with its prolapse of the floppy epiglottis or arytenoids into the laryngeal glottis with each inspiration. Inserting a laryngoscope will not relieve obstruction from bilateral abductor paralysis of the vocal cords, stenosis or atresia of the larynx or laryngeal web, papillomas of the larynx, or subglottic hemangiomas. Insertion of a 3.5 mm. bronchoscope at this point will improve the situation in these laryngeal problems, but it will not relieve tracheal obstruction until the bronchoscope is passed beyond the point of obstruction. The manipulation described here is of utmost danger to a newborn even in the most experienced hands. It should not be undertaken unless the infant's exchange is inadequate for survival. In general, if the exchange is adequate but noisy, it should be treated expectantly in the neonatal period. Most forms of congenital stridor improve with time. Inappropriate instrumentation may convert a tolerable degree of airway obstruction into one requiring a tracheotomy. A tracheotomy in a newborn is hazardous technically and extremely difficult to manage from a nursing point of view. Except in the case in which exchange is inadequate for survival, an infant is in more danger of sudden asphyxia after a tracheotomy than before the tracheotomy. The mortality and morbidity of tracheotomy in an infant due to the procedure, exclusive of the underlying disease, are well documented.[10]

However, if the exchange in a newborn is inadequate for survival due to a laryngeal or tracheal abnormality, tracheotomy is mandatory. The insertion of the bronchoscope past the obstruction converts the emergency to a more orderly situation for performance of the tracheotomy.

Respiratory distress associated with feeding and accompanied by dysphagia should raise the question of a tracheoesophageal fistula. Radiographic proof of this anatomic abnormality can be obtained with a swallow or instillation into the esophagus of iodized oil. Endoscopic attempts at diagnosis have no place in this condition. In the presence of noisy respiration but

adequate exchange in a newborn in whom esophageal atresia and tracheoesophageal fistula have been excluded by an iodized oil swallow, expectant management is in order for the neonatal period. Most forms of laryngeal stridor will improve in two to three months.

In those cases in which the stridor persists for two to three months without improvement or is getting worse, endoscopic evaluation is in order. Bilateral abductor paralysis of the vocal cords due to birth trauma and the exaggerated infantile larynx are likely to have improved by two to three months of age. Stenosis and atresia of the larynx and laryngeal webs are likely to have remained constant in their degree of respiratory distress. In the management of these laryngeal lesions, extreme conservatism surgically is mandatory. These lesions do not lend themselves well to early surgical reconstruction of the larynx. The best results are obtained when considerable growth has been obtained. Early surgical intervention is likely to produce an annular cicatrix, which will make ultimate repair more difficult. A permanent tracheotomy may be required.

Progressive stridor of the laryngeal type suggests the possibility of laryngeal papillomas and subglottic hemangiomas. These lesions usually require tracheotomy at some time during their natural history. Laryngeal papillomas should be removed endoscopically very gingerly. These lesions cannot be cured by endoscopic removal. Care must be used to remove only the papillomas and to avoid injury to any normal laryngeal mucous membrane, musculature, or cartilage. The purpose of removal is to improve the voice and airway. Resolution of the process depends on the natural history of the disease, which is usually gradual cessation of the growth of these tumors with age. Ordinarily, this cessation of growth occurs by puberty. At that time, if the removal of the papillomas has been atraumatic, the individual is likely to have a normal voice and airway.

Subglottic hemangiomas appear as purplish masses just below the true cords. They are likely to be asymptomatic until the infant has his first upper respiratory infection. They should not be biopsied because of the likelihood of uncontrolled bleeding into the trachea. External radiation to a tumor dose of 400 to 800 r offers the best form of therapy reported to this time.[11]

Tracheomalacia is recognized endoscopically by the improvement in exchange that occurs once the weak area is passed by the bronchoscope. Tracheomalacia improves with time. Tracheal stenosis is recognized by the inability to pass a bronchoscope of appropriate size for the age of the infant beyond it. Absence of tracheal rings appears as stenosis, but the bronchoscope passes it easily. Absence of tracheal rings and tracheal stenosis are rare, but difficult, pediatric surgical problems.

Tracheoscopy may demonstrate a pulsatile compression of the anterior or lateral walls of the trachea due to the vascular ring malformations. Tracheography will also demonstrate the tracheal compression. Angiography definitely delineates the type of vascular ring present. The results of division or reposition of these vessels are usually good.[12]

The most common cause of stridor coming on later in the first two years of life is infectious laryngotracheobronchitis and epiglottitis. These acute processes may be due to viral agents or to bacteria. Their onset may be sudden, and the degree of respiratory obstruction may be severe. Humidification of the inspired air is symptomatically very helpful. Usually the use of humidification reduces the respiratory distress in a matter of only a few hours and often obviates the need for a tracheotomy. Treatment of the underlying bacterial infection is in order and reduces the overall length of the illness but probably plays little role in the initial relief of the respiratory obstruction. The value of antihistamines and corticosteroids in the management of croup has not been proved.

Epiglottitis is more likely to require tracheotomy than laryngotracheobronchitis. Its onset is more sudden and its resolution is less reliably related to humidification of the patient's atmosphere. Sedation is to be avoided. Depression increases the infant's difficulty in coping with the mechanical problem of adequate respiratory exchange. Frequent observation of the pulse and respiratory rate is important in making the decision for tracheotomy in the infant who does not respond to these measures. A rising pulse rate, particularly above 140 per minute, is an ominous sign of cardiorespiratory decompensation. It is often more indicative of the need for a tracheotomy than a rising respiratory rate.

In the infant with croup who presents in extremes or becomes progressively worse with the signs of fatigue, a tracheotomy is performed more satisfactorily by converting the emergency to a more elective procedure, by either inserting a bronchoscope or an endotrachial tube into the trachea. A manageable airway is quickly provided in this way. General anesthesia can be administered to allow the tracheotomy to be performed in a precise manner, free from strug-

gling. The tracheotomy in a relaxed infant is less likely to be complicated by pneumothorax and the other technical complications of the procedure.

Stridor and respiratory distress coming on suddenly in an otherwise well infant, not proceeded by a respiratory tract infection, makes a thorough search for a foreign body mandatory. Unfortunately, radiographic demonstration of the foreign body of the upper and lower respiratory tract or of the esophagus cannot always be made. Exclusion of the possibility of a foreign body can only be made endoscopically. However, premature endoscopic manipulation in a primarily infectious process is likely to result in an otherwise unnecessary tracheotomy.

Another cause of sudden stridor and respiratory distress in an infant is trauma to the larynx. The underlying etiology of the stridor is frequently overlooked.

Infants with retropharyngeal abscesses usually present with stridor and hyperextension of the neck. They are febrile and toxic. In the presence of a normal cerebrospinal fluid, the possibility of a retropharyngeal abscess must be excluded. Lateral roentgenographic views of the neck are helpful but may be difficult to interpret, in view of the relatively thick retropharyngeal space normally demonstrated radiographically in an infant. Palpation of the posterior pharyngeal wall with the index finger with the infant face down is the most reliable means of establishing this diagnosis. Ordinarily, the bodies of the cervical vertebrae can be palpated distinctly. In the case of a retropharyngeal abscess, the retropharyngeal space is soft and boggy without sharp bony detail. Prompt incision and drainage through the posterior pharyngeal wall under general anesthesia will ordinarily circumvent a tracheotomy.

SUMMARY

The physical characteristics of the various portions of the respiratory tract important in airway obstruction are reviewed. Salient points in the differential diagnosis of the site and the etiology of the stridor are discussed. The gathering of as much information about the patient as possible, in preparation for endoscopy, is emphasized. The diagnosis and management of the causes of noisy respiration are discussed.

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Learning Problems of Handicapped Children

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THIS ARTICLE is an attempt to explain some of the factors encountered by handicapped children which help produce difficulties in learning. Under the classification of "handicapped" there are included a wide variety of disorders. There are those that involve the perceptual system such as blindness, deafness, or certain neurological diseases. There are those that involve the motor system either directly or indirectly through injury, disease of the central nervous system, or through orthopedic deformities. There are those involving the cardiac or respiratory systems which result in a decrease in performance capacity. There are cases of mental retardation which are related to heredity, prenatal or postnatal influences, or of unknown causation. Finally, there are innumerable other diseases that can cause brief or prolonged incapacity.

Besides the multiplicity of possible causative factors of handicaps, there are series upon series of enormously complex and interrelated possible emotional reactions. What is to follow will be a brief survey of what we know about neurophysiology and psychology that has a direct bearing on the learning difficulties of the handicapped. The model constructed will have the obvious defects of oversimplification, but it is hoped it will serve to illustrate graphically the nature of the problems involved in the teaching of the handicapped.

NEUROPHYSIOLOGIC "GIVENS"

Unless there is some process that interferes with intrauterine development, there are many neurological potentials with which the individual is born. These are the "givens" in each person; for example, the ability at birth to participate in life with reflex actions such as sucking, rooting, grasping, crawling, and walking. It also includes the ability at birth to have coordinated movements of the head, eyes, and torso. It includes the potential for later development of the ability to speak, to judge, to remember, and to abstract.

In order for these later functions to develop and to remain stable and consistent, the central nervous system needs a constant level of stimulation.[1–7]

There are many proofs of this need of the central nervous system for constant stimulation. Babies who are not stimulated, particularly by emotional stimuli, often waste away and die with marasmus.[8–10] In recent experiments relating to isolation, visual, auditory, and kinesthetic stimuli have been withdrawn and in a relatively short time, even the most normal adult begins to talk to himself, feel everybody is against him, and have auditory, kinesthetic, and visual hallucinations.[11,12] Thus, even where the ability to judge, remember, and abstract have been well established, they can be interrupted and the individual will regress to much more primitive methods of functioning.

It is on the basis of repeated stimuli from all the perceptual apparatus—visual, auditory, kinesthetic, pain, pressure, smell, temperature—that memory traces or the fundamentals of all learning take place. These memory traces or habit patterns are dependent upon the establishment of cortical reverberating circuits.[13–18] An incoming stimulus will automatically set in operation electrical connections between the cells of the brain which will establish recall or memory. An infant will hear and see his mother, be held by her, rocked, fed, stroked, and talked to. Thus, he is able to materialize the image of his parent. This image is made secure by the constant repetition of this process. The connections between the various nerve cells require these constant, repeated inputs to establish recall. In this particular way, through the association and reinforcement of the reverberating cortical cellular circuits, the child is able to leave its parents for moments of time and recollect by himself the way the parents look and act and want the infant

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to act. This image is fairly well established by 6 to 8 months so that when a stranger approaches a child of this age, the child cries since the face is not that of the expected gratifier of internal tensions. This has been noted clinically and called by Dr. Renee Spitz "the eight-month anxiety."[19]

This bond between parent and child can be interfered with when all of the systems are not intact, in which case the internalized image is poorly established. In the blind child, daydreaming and hallucinations and disregard of external reality occur because the child has not had sufficient reinforcement of the parental images by one of the important input mechanisms, sight. The same is evident in other sensory disorders. Poor internalization of the parental image is also caused by parents who, because of their own feelings of disgust, repulsion, and shame, do not involve themselves intensely with their handicapped child and thus stimulate all the available sensory inputs.

Firm object relationships are interfered with continuously in many of the handicapped by repeated and prolonged stays at hospitals. One of the major results of strong ties to parents is the ability to contain, restrain, and channelize for appropriate discharge, overwhelming feelings of anger and anxiety. It is therefore true that in the individual who has not formed this close bond to the parent, that individual would be subject to outbursts of rage or bursts of anxiety or its equivalents such as nightmares, confused thinking, and somatic symptoms.

A good example of the functional power of close ties with the parents can be seen in the accidentally artificial experimental group situation that developed in England during World War II. At the time of the "Blitz," children were evacuated from London and went to fine foster homes—quite psychologically sound and physically safe—in other parts of the country. A study conducted fifteen years later revealed that those children who were evacuated and kept in the safe places, but separated from their parents, had suffered with emotional problems to a much greater extent than those left with their parents in London, even though the physical threat and the air of emotional tension was so much greater.[20]

Among the other neurophysiologic "givens" is a sort of circuit-breaking mechanism in the central nervous system, probably part of the reticular formation. This prevents overloading the personality with too many inner or outer stimuli. Freud, noting this clinically, called this psychic barrier the "Reizschutz."[21] A most obvious example occurred each time an 18-month-old boy would go to the cast room to have his cast changed. Of all the areas that are upsetting in the hospital, the cast room is considered by the children to be the worst. Despite all the reassurances or demonstrations given by the residents, the cast saw has a terrifying, loud noise. More crying and outbursts of fear go on before the harmless removal of casts than before surgical operations or painful manipulations. The terror of the children was so universal that each child was brought down only after the one before had already left. One day the orthopedic residents called me down to witness an event that they felt would disprove, once and for all, the universality of the child's fear in the cast room. They brought down a delightful 18-month-old boy who had been in the cast room many times before. With glee and expectation the residents had brought him in and demonstrated conclusively that as the child passed from the corridor into the cast room, he fell into a deep, profound, unarousable sleep. Through the entire time it took to remove his cast, he slept undisturbed by noise, movements, speech, or complete changes of position. The residents' interpretation of this was that the child was so at ease he could sleep. It was quite remarkable, but still pathological, as proved by his immediate awakening without any outside stimulus, as soon as he passed through the door from the cast room into the hallway. He wasn't unafraid, nor had he built up a nonchalant tolerance by virtue of frequent exposure. He was overwhelmingly frightened, as proved by subsequent experiences, and his circuit breaking mechanism had him retreat into sleep—a kind of autohypnosis. Fainting with bad news or a broken leg is another method of keeping the personality from being overloaded.

In the handicapped, especially those who are deformed, we see a tremendous increase in fantasy life. This is their retreat from being looked at, as one boy said, "as if he were a monster." This, too, is the basis for many children withdrawing from contact with others, except, as often seen in my experience, others who are of their kind. We have often heard the children say that they'd like to stay longer in the hospital or come back again very soon as it is here that they feel comfortable. Everyone of them is in a glass house and they dare not throw stones. Or conversely, in the hospital situation, they can be kidded, just as they can afford to kid back, without the fear of hearing some devastating remark about their own deformity.

PSYCHOLOGICAL "GIVENS"

Many emotional problems are based upon the conflict between elements in the personality that are labeled good and bad. The physical model from which this stems is the eating of that which one likes and the ejecting of that which one does not like. It is important to note that when one eats something, its form and substance is destroyed and, of course, if it is ejected, it is destroyed as a valued object. It is surrounding these destructive feelings that we see the major defensive mannerisms and pathological states.

This can be seen in all phases of life. Even in the classically described Oedipus complex, it isn't the tender loving feelings for the child's mother that creates problems, but rather that in order to be number one with her, the child has to rid himself of his father. The anxieties about destroying his father, whom he loves too, are coupled with fears that father, being bigger and stronger, would not take being replaced too kindly. It is this that creates conflicts in this period. Also present in all human beings are greedy, selfish, and covetous desires that constantly seek satisfaction and are often thwarted by outside objects. To get what one wants requires the destruction, or certainly the frustration, of others. Telling people to count their blessings hardly ever works as they rarely compare themselves with those who have less but rather always find those who are more fortunately endowed. This is one of the bases of the family romance when children imagine they are adopted by their present parents but in reality are the child of a king and queen.

In the handicapped, comparisons are readily available to them to demonstrate how much better off others are. They tend to become depressed and angered, withdrawn from reality into fantasy, blaming all of their difficulties on the handicap.

Psychologically the child needs to imitate—to identify eventually with others about him. He can identify with the whole or parts of people and can, therefore, have even diametrically opposed ideas coexisting. Thus, the personality becomes a gigantic jigsaw puzzle composed of many parts of many outside people. It is this tendency to pick up, and then internalize attitudes, that helps to explain some of the attitudes of the handicapped child toward himself. Handicapped children become aware of the looks, the attitudes, and the intonations of people in their environment toward their handicap. These things they internalize and, therefore, can develop extremely negative attitudes toward parts of their own body. Conversely, the injured member becomes prized as it is often the central topic of conversation and interest, as well as the focal point of attention, of everyone in the entire environment. It is protected and guarded and even becomes the excuse for actions. The example Shakespeare used of Richard III is seen repeatedly. Mother Nature played a dirty trick on him and he had this excuse to do as he pleased. This is reinforced often by people in the environment who, in an attempt to compensate for fate's adversities, become overly permissive and lenient.

It must be remembered that children think concretely. Because of their lack of knowledge and experience they often form incorrect conclusions that remain imbedded in their unconscious and conscious thinking until something happens to explain it the right way. A three-year-old boy was going on a vacation with his family. They were to go on an airplane, the first time for this child. All was well until they were about to board the plane. The child suddenly became hysterical and uncontrollable. Since this was so unusual for him the parents were amazed and confused. It was not until his father took him back into the building that the boy calmed down enough to explain the reason for his violent reaction. His impression was that if he got on the plane, it would fly into the sky with him, get smaller and smaller, and finally with him and the rest of the family aboard, they would all disappear—and he didn't want to disappear. We can see from this example that adult logic doesn't always work. The child needs more explaining and looking at things from his own point of view. Many times this is difficult because the child often does not have the verbal ability to explain his position so that the adults are able to correct a misconception.

To be able to think clearly and correctly enables the child to master many fears. To be able to walk and to see the world also help to conquer the unknown; to be in a position where he can make relationships outside the family helps the child master the fears of breaking away from the family and become an independent, self-sustaining individual. The handicapped child is much more hampered in these independent strivings. The mentally retarded, the deaf and mute, often have real problems in learning speech which is used to conquer ideas and feelings. The cardiac, respiratory, orthopedic, blind, or central nervous system damaged child remains confined to small areas of his home so that he is unable to see that the outside world is not so frightening or bizarre. He is, in a much greater way, forced to remain with the ideas neurotically determined

or otherwise of his family, and not have as free a choice of concepts, frames of reference, or different approaches to life's problems.

STAGES OF PSYCHOSEXUAL DEVELOPMENT

As the child develops, the neurophysiological and psychological "givens" are molded and influenced by his external and internal environment.[22] During certain stages of development, particular organ systems predominate in importance as far as awareness, modes of use, and discharge of tensions. Conflicts occurring during these periods are colored by the thinking that is predominant for that stage of growth. For example, fears during the oral phase are expressed in terms of being eaten up. Fears during the anal phase are experienced in terms of being flushed down the toilet. Fears during the phallic phase are expressed in terms of bodily mutilation. Therefore, any handicap that occurs during the ascendency of one of these phases of development is colored in the child's thinking, by the major area of emotional involvement. The children with congenital defects, or those acquired during the first year of life, are often extremely dependent, always talking and demanding, and never able to give. Those whose defect occurs during the second year of life are often stubborn, bitter, and antagonistic. Those with defects occurring in the third to fifth year are often constantly anxious and fearful or aggressive and belligerent. If the defect occurs later, the child can slip back to any one of these characteristic ways of reacting, depending on his general personality makeup. These traits have to do with the influence of the child's internal environment.

It is the influence of the external environment that many times affects the attitude the child takes toward his own defect. If the parent feels the defect is caused by the child or parent having sinned against God, there will be a persistent guilt feeling. Parenthetically, this is reinforced by the psychological tendency to view things in terms of good and bad. The child feels, "if there is something wrong with me it must be the result of a punishment that I received for doing something wrong." Some 80% of the children over age 5 seen in an orthopedic hospital compared with 5 patients who had congenital or acquired defects due in no way to any fault of their own, attributed the deformity to some misdeed or accident caused by their own naughtiness.

Society shuns the handicapped and adds further to their feelings of not being a part of things. The handicaps give rise in normal people to fears of the same thing happening to themselves. Parents of the handicapped children have been heard to say that nothing was wrong with their child when asked by outsiders what was wrong with an absent arm or paralyzed leg. For the child, this distorts his reality testing. Part of him would like to believe his parents since he loves and trusts them. Besides he, too, would like to believe nothing is wrong. Yet, no matter how strong these ties and desires are, his perceptions tell him differently.

TYPE OF HANDICAPS

Certain responses occur more regularly with the type of handicap the child has, depending upon the age it occurs. In the blind child, there is a real difficulty with testing reality. It is much more difficult to tell what is frightening or what is destructive that might be coming toward him. He needs to rely on external objects to protect, as well as to check, reality for him. Since the incoming stimuli are absent from the visual centers the blind must stimulate themselves, which accounts for autisms, odd mannerisms, and the weird fantasy life usually seen. Relationships to people are often tenuous.

In the deaf and mute, there is a tendency toward suspiciousness bordering on the paranoid. "What are people talking about? Are they talking about me? Are they saying unkind or threatening things?" Since word formation is not as easily developed, we see a corresponding lack of adequate control over feelings.

With difficulties of the motor system, the child lacks the ability to master space. They also cannot master aggressive destructive impulses that are most frequently discharged through large motor activities. Their world is more constricted and, therefore, their thinking is, too. Their dreams are of being chased by monsters, as it is with most children. The only difference is that they get caught because, even in their dreams, their deformity exists and they cannot run fast enough. So we see a tendency to ever-present anxiety.

This is true, too, in certain cardiac, respiratory, and orthopedic problems. These children are not only unable to physically move rapidly from place to place, but they also are faced with the ever-present danger of overexertion that can lead to severe injury or even death. These children treat themselves like fragile eggshells, capable of being crushed by any inopportune move.

The mentally retarded often suffer from constant anxieties. Their thinking is limited and concrete. They cannot understand abstractions or complexities and so potential danger lurks anywhere and everywhere. What was a fear early in life, remains a fear. They are not able to be

as influenced by logic or by developing new concepts to help correct such early misconceptions.

EFFECT OF HANDICAP ON LEARNING

Since the constant efforts of parents, the care from physicians, and the prayers to God fail to effect removal of the handicap, many of these children develop a pervasive and deep feeling of the uselessness of life. This feeling of hopelessness affects all activities and results clinically in profound depressions, especially in the adolescent. The deformity often is seen as the mark of Cain, an external evidence of their badness; so punishment is their fate. Pleasurable activities which include learning are to be denied. They are so preoccupied with the handicap that little energy is left for other activities. Fantasy is more pleasurable and easier, so that it preempts all of the thinking processes. They fear all kinds of experiences and look at learning as another area in which the shame of failing (for example, being deformed) will occur again. Learning is involved in a symbolic way, too, with their handicap. A number of children do very poorly in geography as it unconsciously represents a discussion of the anatomy of the world and they do not want to know about anatomy because it is too unpleasant.

There are differences in the way we all learn. Some people are primarily auditory learners, others visual, others kinesthetic, others a combination of these. In the handicapped child a significant portion of their input or perceptual systems are not available to them to form and reinforce the associations in the central nervous system. Teaching by methods advanced by Montessori and others attempts to make use of whatever auxiliary input systems are available to them to increase memory and awareness.[23]

With the child who has visual or auditory defects, we need to emphasize and repeat other modalities to make the central impressions stable. In the mentally retarded, we need to repeat and repeat with the use of all modalities, as the engrams of learning are not as easily layed down. In the handicapped whose motor system is impaired, reinforcement must be obtained from areas besides kinesthetic and vibratory unless the teacher can actually stimulate these systems with the child being the passive recipient. Systems devised by Delacado,[24] such as crawling, and Kephart,[25] with the use of the trampoline, to increase awareness, for example, of which side is which, need to be applied since these children try desperately to block out awareness of, and have impaired ability to know, their own distorted bodily limits.[26]

Primarily, since teaching of all kinds depends upon adequate object relationships, it is incumbent upon the teacher to find methods of working and maintaining contact with the child, irrespective of which perceptual system she uses to enter his awareness. The handicapped child, even more than the normal child, must have an educational program built individually upon his own special needs and abilities. Educational, pediatric, and psychiatric conformity can be destructive in these children as their handicaps are so varied and their need so individual. Each child should have the opportunity of a team evaluation that properly should include the pediatrician or family physician as its chairman. Other team members would be the medical specialist most involved with the child's problem (for example, orthopedist, ophthalmologist, otologist, neurologist, and such), a pediatric psychiatrist, a psychologist, a teacher from special education with some administrative authority, and a consultant trained in vocational rehabilitation. A conference of all of these people concerned with an individual child should produce a current evaluation of the abilities and potentials, as well as a statement about the child's limitations. Recommendations should be made on the basis of this cross-sectional appraisal for medical and paramedical procedures to improve current functioning. Recommendations for handling the child at home, school, and institution would be part of the outcome of such a conference. Hopefully, parents and educational institutions would attempt to modify standard procedures to fill the need of each of these handicapped children. Reevaluation and follow-up should be built into this type of programming so that new suggestions in the future could take into account changes in the child, as well as newer procedures available. With this type of total evaluation and planning, these children and their parents will need to receive less help from public funds but, more importantly, will grow into adults who are returning value to their society and developing, in themselves, feelings of accomplishment and self-worth.

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Language Disorders in Children

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RECENT medical, psychological, and educational literature reflects an increasing interest in children with language disorders. It has been estimated that approximately 5% of the preschool population has language disorders severe enough to impede speech development and complex enough to require professional attention.[1] Among school-age children it is estimated that approximately 10% have language disorders severe enough to interfere with the learning of reading and writing, as well. These children may also show behavioral symptoms of cerebral dysfunction, which are often termed "organic behavior disorders." The language problems and learning disabilities related to such neurological impairment are sometimes classified as neuropsychiatric (or psychoneurological) learning disorders.

Major attention in the past has been directed to oral communication: peripheral and central auditory sense functions and the motor functions of speech. Language, however, embraces a broader concept of sensory-motor functions, as well as communicative or social. On the side of sensory in-put, the visual and kinesthetic senses are involved, as well as the auditory, in language development. As hearing is to spoken language, vision is to reading. As speech can be considered the motor function of spoken language, writing can be considered the motor function of reading.

The term "language disorders" refers to the inability, or limited ability, of a child to use spoken and written symbols for communication or both. Dysphasia is concerned exclusively with an inability to receive or express spoken symbols. Dyslexia indicates a problem in the reception of written symbols. Dysgraphia refers to a problem in the expression of written symbols. Thus, developmental dysphasia, dyslexia, and dysgraphia all represent disturbances in the development of particular language functions.[2] They are closely related conditions and are often found together in the same patient or in members of the same family. There are many points of similarity in their etiology and clinical pictures. In each, the process of symbolization is impaired. Yet, there is a tendency to regard them as discreet clinical entities, and particularly, to explain dyslexia and dysgraphia in terms of "lateralizing confusion" or to attribute them to "mixed hand and eye dominance." The fact is too often ignored that specific developmental dyslexia and dysgraphia, like developmental dysphasia, are disorders of language.

At present, there is a strong concensus that language disorders in children are caused by central nervous system dysfunction, characterized minimally by a perceptual immaturity or developmental lag, or by perceptual disorder. In severe cases, marked neuropathological signs and neuromotor impairment may be seen.

As components of a continuum, behavior disorders and symbolic learning disabilities caused by minimal cerebral dysfunction usually exist together in varying combinations, but they may occasionally appear independently. Characteristic of this impairment is absence of specific neurological signs, although minor degrees of motor incoordination, nonspecific awkwardness or clumsiness, crossed laterality, time and spatial disorientation, or adiadochokinesis can usually be detected. Retarded development of speech, dyslalia, echolalia, strabismus, visual-motor impairment, and abnormal electroencephalograms may be found in greater numbers of children with developmental language disorders than in control subjects.

In the very young child the major manifestation of dysphasia is retarded development of speech. Symptoms may include failure of speech development, failure of auditory comprehension, and possibly clues with regard to central nervous system involvement. These, along with an abnormal birth and neonatal history or both, may add to a presumptive diagnosis of dysphasia and would be particularly significant if there was relatively normal development in other areas. The differential diagnosis of dysphasia must include other disorders which cause significant

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retardation of speech development such as hearing loss, intellectual subnormality, and severe psychiatric disorders. Neurological or structural abnormalities affecting the articulatory organs, and gross uncomplicated environmental deprivation, rarely cause serious retardation of speech development, and when they are severe enough to do so they are usually obvious even in the most overworked pediatric clinic.

It may be extremely difficult to distinguish hypoacousis or impaired hearing acuity from dysacousis or central auditory imperception. Young children with either tend to rely on gesture and to lip-read. Fortunately, by the time children suffering from dysacousis reach the physician or the speech clinic, appreciation of sounds other than those of speech may be apparent. A positive family history of retarded speech development or of reading and writing difficulties, or of sinistrality or ambidexterity without abnormalities of hearing, may be helpful clues. Definitive diagnosis must depend on detailed clinical and audiological examination.

Children who are intellectually subnormal may present clinical manifestations similar to those of dysphasia. Patients with either condition may show inattention to the spoken word, relatively normal motor milestones, and grossly retarded speech development. It is not uncommon for mental retardation and developmental dysphasia to be associated in the same patient, the dysphasia made more apparent by the child's relative inability to compensate for it. Although a history of uniform retardation in motor, adaptive, language, and social aspects of development is in favor of the diagnosis of intellectual subnormality, many retarded patients will show remarkably normal motor development, and their backwardness in adaptive and social behavior may be ignored by doting parents.

Gross phychiatric disorders are rare in very young children, but autistic children may be very late in speaking; their inattention to speech and other environmental sounds may suggest deafness or intellectual subnormality. However, it is more common for children with severe dysphasia and secondary withdrawal reactions to be diagnosed as showing "autistic traits" by eager psychiatrists, than for autistic children to be diagnosed as dysphasic.

Similar problems to those found in the diagnosis of dysphasia in childhood occur with dyslexia and dysgraphia. However, these disorders in symbolization are usually not apparent until the child is in school and are frequently overlooked until he is in approximately the third grade.

Before assuming that slow speech development, or clumsiness, or specific difficulties in writing or reading are the result of brain dysfunction, it is well to remember that there is a wide distribution of ability in children. For example, though the vast majority of children have IQ's between 90 and 110, some normal children are well below average and some are above average intelligence. Similarly, while some children are very dextrous, others show less than average dexterity and may be called clumsy. Some apparently normal children say their first words before the age of 9 months and others may not speak until over the age of 2 years.

Secondly, it must be remembered that many of these disorders can occur in generation after generation of apparently normal children. For example, slow speech development and specific difficulties in reading and writing, often associated with ambidexterity or poor lateralization of handedness, are relatively common in the families of Campbell and Maclean in Scotland. It is difficult to attribute the symptoms and signs in such familial cases to "brain damage" as this term is commonly understood.[2]

Neurologists who are chiefly concerned with adult patients tend to think in terms of focal cerebral lesions to account for specific speech and learning difficulties in childhood. Thus, a child who is clumsy and not obviously paretic or ataxic is considered to show developmental dyspraxia by Walton. The child's failure to develop accurate movement patterns is equated with loss of movement patterns which occurs in adult patients as a result of specific focal brain lesions.[3] Similarly, a child's slowness to speak, where there are no difficulties in comprehension, may be equated with expressive dysphasia in the adult; and slowness to speak where there are difficulties in comprehension may be equated with sensory or receptive dysphasia and the adult.[4] Actually, it is rare to find focal lesions of the brain in childhood associated with the neuropsychiatric disorders included in this category.

A major factor, often ignored, is the influence of environmental factors in producing specific clinical manifestations. A high proportion of children with retarded speech development, for example, have a history of being neglected by, or separated from, their parents in later infancy.

Mental retardation, visual defects, severe psychiatric disturbances, or psychogenic stress may all interfere with the processes of learning to speak, read, and write. In any of these conditions the case history may indicate encephalopathy as the probable cause of the disability. In other cases, no such history is found and the disability

may be due to a developmental neurological deficit or immaturity. Detailed history-taking and careful physical and psychological examinations usually will clarify the diagnosis.

It is important to recognize that many children with language disorders, the nature of whose handicaps are not well understood, are being treated in child guidance clinics, remedial reading centers, speech correction classes, and special educational settings, although they have never been adequately studied and have not responded well to long-term and intensive intervention. Speech therapists are treating children for mechanical speech defects when, in some instances, a profound central language disorder exists. Known bright children with specific reading disabilities have been managed for long periods of time on the presumption that they were poorly motivated, "emotionally blocked," or neglected at home. Intelligent children with reading disabilities are often considered mentally retarded on the basis of group intelligence tests which presuppose the one skill which is notably impaired. The usual neurological examination is sensitive to less than 50% of brain function, yet many clinicians have excluded the possibility of any central nervous system dysfunction on the basis of this type of examination alone.

The inherently complex nature of the problems of children with language disorders crosses many professional boundaries. In the study of these children we are continuously aware of our lack of knowledge in all fields. We are further hampered by assumptions based on clinical findings in the adult who has acquired a language impairment. It must be remembered that in the immature, developing organism malfunction in any area will have a different effect than it would in the mature organism. More objective methods must be found for studying language patterns and for understanding them. The most urgent need is for early recognition of children who have language disorders.

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The Relative Role of Heredity and Environment in Congenital Heart Disease

A Review

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MOST CONGENITAL malformations are the result of complex interactions between multifactorial genetic and environmental systems. The normal growth and development of a fertilized ovum depend both on a normal complement of genes and a normal maternal environment. Disturbances of development are most likely to develop in a zygote which is particularly susceptible to certain changes in environment because of its genetic constitution.

It is the purpose of this paper to examine the role that both genetic predisposition and environmental factors play in the pathogenesis of congenital cardiovascular malformations. It is not intended to present an exhaustive coverage of the subject but to search for valid generalizations and basic principles that may be deduced from the experimental data now at hand.

EVIDENCE FOR GENETIC FACTORS

The classical methods to demonstrate the operation of genetic factors are familial aggregation studies, twin studies, pedigree analysis, the consanguinity method, and chromosomal studies.

Family aggregation studies. An increase in the incidence of congenital heart disease among siblings and other relatives of affected individuals as compared with the incidence in the general population would point toward a genetic etiology. Several recent studies have examined this question.[1–6] In general, it can be shown that siblings of patients with congenital heart disease have approximately 3 times as many heart lesions than are found in the general population. When subgroups of lesions are considered separately, the incidence of similar lesions in siblings varies all the way from no increase over the general population, in the case of coarctation of the aorta,[7] to a sevenfold increase, in the case of pulmonic stenosis.[3]

Interestingly enough, although an increase in incidence can be demonstrated for siblings of the proband, a similar increase cannot be shown for parents or other relatives of the proband. The important question of what is the reproductive history of the growing number of patients with cardiac defects corrected by operation was first raised by Weinstein[8] and subsequently studied by Neill and Swanson.[9] It was found that the incidence of congenital heart disease was increased sixfold in the offsprings of a group of women who themselves have congenital heart lesions. Also, an extremely high (60 to 85%) abortion rate was noted in mothers with cyanotic types of heart disease. This, once again, does not help one decide whether this is evidence for nature or nurture in the pathogenesis of the observed defects.

It is of some significance to mention that there is a demonstrable increase in the overall frequency of all types of congenital defects in the family of a patient with congenital heart disease,[3] which would lead one to believe that the genes responsible for causing abnormalities in the cardiovascular system probably are nonspecific in nature and, depending on their timing and interaction with other genes and the environment, determine many different kinds of growth aberrations in the developing fetus.

Twin studies. Usefulness of available data in this area is seriously limited, due to bias in selection of cases. On the whole, the published twin data suggest a much greater importance of extrinsic factors than genetic factors in the etiology of congenital heart disease. Since monozygotic twins have a much greater genetic similarity than dizygotic twins, the concordance rates should be significantly greater in the monozygotic twins if genetic factors are important in causing congenital heart disease. Absence of any dissimilarity in

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concordance between monozygotic and dizygotic twin pairs is a consistent finding in the available twin data (Table 1). Of course these data con-

TABLE 1
TWIN STUDIES OF HERITABILITY OF CONGENITAL HEART DISEASE

	Concordance rates			
Investigator	*Monozygotes*	*Twins*	*Dizygotes*	*Twins*
Lamy and associates[3]	0/5	(0%)	1/8	(16%)
Uchida and Rowe[11]	0/13	(0%)	0/13	(0%)
Ross[12]	2/11	(18%)	2/24	(8%)
Totals	2/29	(7%)	3/44	(7%)

Modified after Pitt[10]

sider congenital heart disease as a single entity. If the above type of analysis were applied to individual defects, the presence of genetic factors might not have been masked by such pooling of mixed data.

It has been suggested that monozygotic twins seem to be more likely to have cardiac malformations than dizygotic twins. Two explanations have been given for the excessive number of monozygotic over dizygotic twins with heart defects. Campbell[13] feels that monozygotic twins with a single placenta and chorion are more likely to have disturbances of the fetal circulation to one of the fetuses. An alternate explanation by Torgersen[14] states that the polygenic complex regulating visceral asymmetry is disturbed in monozygotic twins, to the point where symmetry (and subsequent congenital defects) occurs. The importance of visceral asymmetry to the development of normal cardiac structures has been pointed out by other authors in relation to the syndrome of congenital absence of the spleen associated with cardiac abnormalities.[15,16]

Pedigree analysis. This technique has been useful in describing the manifestations of single major genes, which behave according to simple laws of Mendelian genetics. Unfortunately, the majority, if not all, of the common diseases are probably determined by a complex polygenic system of inheritance which does not lend itself to pedigree analysis.[17] There are, however, selected cases of congenital heart disease which seem to be controlled by single gene systems:

1] Genetic syndromes, or a group of diseases which could be termed heritable disorders of connective tissue, are known to include significant cardiovascular abnormalities.[18] Included in this group would be the Marfan syndrome and the Ehlers-Danlos syndrome, both associated with aortic aneurysm, Hurler's syndrome associated with endocardial fibroelastosis, and the Ellis-van Creveld syndrome associated with cor triloculare. It would seem reasonable to assume that the various types of heart defects listed above are secondary to basic mesenchymal defects which characterize the various connective tissue syndromes and are therefore under direct genetic control. Less well understood syndromes, such as congenital asplenia with dextrocardia[15] and mental retardation with supravalvular aortic stenosis, are probably due to major gene action but modified by a threshold effect, which makes an analysis of affected pedigrees difficult.

2] Phenocopy, or pedigree analysis of the miscellaneous groups included in any one clinical category of congenital heart disease, reveals certain families in which a specific lesion is found in several generations and generally behaves as a Mendelizing trait.[1,3,19] Such cases are, of course, in the great minority but do point to the fact that it is possible for each of these specific defects to appear at times under strong genetic control. Apparently, in these isolated cases, environmental factors play a very minor role.

The paucity of documented parent-child constellations of defects could in part be due to the natural history of the disease. In most types of severe congenital heart disease the course is such that the patients do not reach adulthood, or if they do, they do not have children. To lend support to this hypothesis, Zetterqvist points out that when identical lesions have been found in 2 successive generations of a family, the defect is usually of a type known to run a mild course during the first 2 or 3 decades.[20]

Consanguinity method. An increased number of consanguineous marriages in the parents of affected children is generally considered evidence for recessive inheritance of the condition. The majority of investigators[3–5] who have examined this aspect of congenital heart defects have found very little evidence of increased consanguinity among parents of affected children except in the case of dextrocardia, where there is roughly a threefold increase in consanguinity.[21] The suggestion has been made by Lamy and associates[3] that consanguinity increases the frequency of all malformations and only secondarily the frequency of cardiac malformations having a strong genetic component. That there is a strong genetic component in the etiology of dextrocardia is recognized by most investigators, but there are reservations in accepting an increased consanguinity rate as prima facie evidence for a recessive mode of inheritance.[22] As Torgersen points out, an increased frequency of consanguineous marriages in connection with family

aggregates of heart disease not obeying any particular Mendelian ratio is strong evidence for homozygosity of a complex of genic modifiers.[14]

Chromosomal studies. Malformations of the cardiovascular system have been frequently observed in certain chromosomal syndromes, including Turner's,[23] mongolism,[24] and the two less familiar autosomal trisomies.[25,26] Chromosomal abnormalities associated with an isolated cardiovascular defect[27] have been reported, although one cannot at present say there is a cause and effect relationship. Further refinement of the techniques of chromosomal analysis may reveal new etiologic relationships between certain chromosomal aberrations and various cardiovascular lesions.[28]

EVIDENCE FOR ENVIRONMENTAL FACTORS

During the organogenetic period of fetal growth, nongenetic factors may interrupt normal growth and differentiation of the primitive heart, so as to cause a cardiac malformation.

In an attempt to determine the role such environmental factors may play in the etiology of congenital heart disease, the following parameters have been examined by various authors: parental age, birth order, sex distribution, seasonal variation, nutrition of the mother, maternal biochemical milieu, and exposure to infectious agents.

Parental age. Correlation of malformation frequency with parental age can be considered either an environmental or a genetic effect. Any correlation between maternal age and congenital malformation is often thought to show that the cause of the malformation is environmental,[29] while a similar correlation with paternal age should indicate a predominant genetic influence.[30] The only congenital heart defect associated with increased parental age is coarctation of the aorta,[31] which has been found to be associated with increased paternal age, but not maternal age. In no other type of congenital heart disease have significant correlations with parental age been demonstrated.[32,33]

Birth order. Examination of the birth order of affected offspring is the usual method for demonstrating the operation of factors in the perinatal environment affecting the incidence of congenital defects. It has been stated that firstborn males have a significantly higher incidence of patent ductus arteriosus than any subsequent offspring.[34] Since difficulties of labor are more common in first than in later pregnancies and closure of the ductus probably depends, among other things, upon adequate oxygenation of the blood, the observed birth order effect suggests the possibility that in some cases patency of the ductus may be due to fetal anoxia during and following delivery.[35] This same hypothesis was arrived at independently by Alzamora and associates,[36] who observed the incidence of patent ductus arteriosus among the villagers living high in the Peruvian Andes. It was concluded that the oxygen environment of the fetus and newborn may be an important factor in the closure of the ductus arteriosus.

Sex distribution. If a disturbed sex ratio (i.e., male:female incidence other than 1:1) is present, there are 4 possible explanations: [1] differential predisposition, [2] differential mortality, [3] errors in sex determination favoring one phenotype over the other, or [4] different manifestations in the 2 sexes.

Since any combination of these circumstances may be working simultaneously to produce a disturbed sex ratio and any one of them can be equally influenced by genetic as well as environmental factors, great care must be taken in interpreting the significance of a disturbed sex ratio in any disease. With these reservations in mind, let us turn to those studies where a differential sex ratio in the incidence of specific cardiac defects has been recorded. Table 2 presents a summary of these findings. To interpret these facts it ought to be kept in mind that mortality from congenital heart disease in general is higher in males in the first five years of life.[37] This would adequately explain the defects which show a gradually increasing excess of female over male cases in each succeeding decade. An alternative explanation, of course, would be that in certain cases more females than males become symptomatic from their disease and present themselves for medical care. There does not seem to be any adequate explanation whatsoever for the defects showing an excess in males over females. It has been suggested, however, that since all the de-

TABLE 2

CONGENITAL CARDIOVASCULAR DEFECTS WHOSE INCIDENCE SHOWS DISTURBED MALE:FEMALE SEX RATIO

Defect	*Male:female ratio*	*Remarks*
Patent ductus arteriosus[3,34]	1:3	
Atrial septal defect[38]	1:2 (all ages)	1:1 ratio at birth
Pulmonic stenosis[3]	1:9	These ratios do not change with increasing age, and there is not any evidence of a differential female mortality.[31]
Aortic stenosis[5]	3:1	
Coarctation of the aorta[31]	15:1	
Transposition of the great vessels[5]	15:1	

fects showing a high male sex ratio are those affecting the aorta here may be a selective "aortic vulnerability" of the male sex.[5]

Seasonal variation. The only two cardiac defects of a congenital nature showing a seasonal variation are patent ductus arteriosus,[34,39,40] where the variation is dependent on any effect that rubella epidemics may have, and coarctation of the aorta,[31] where only the incidence in males seems to show any seasonal variation.

Nutrition of the mother. Interest in the possibility that nutritional deprivation during the early months of pregnancy may be responsible for cardiac defects in the fetus has been stimulated by Pitt,[41] who showed that mothers with diets poor in niacin had an excessive number of infants with congenital heart disease. It must be admitted, however, that a direct causal relationship between the mother's nutrition during her pregnancy and any subsequent congenital malformation of her infant has not been established in man,[42] although Wilson and Warkany[43] have recorded in the offspring of vitamin A–deficient rats a series of cardiac defects and aortic arch anomalies.

Maternal biochemical milieu. There are two instances where the biochemical environment of the mother seems to exert a strong teratogenic influence on the development of the fetal heart. First, congenital heart malformations seem to be more common in children of severe diabetic mothers as contrasted with children of mildly diabetic mothers.[44] This is not a genetic influence, since malformations are not more common in infants of a diabetic father and a nondiabetic mother.[45] Whether this maternal teratogenic effect is by way of hypoglycemic episodes or by some other mechanism has not been determined. Secondly, the recent experience with thalidomide has emphasized to physicians the potential harm that can come to the developing fetal structures from supposedly innocuous chemical substances. Parenthetically, it might be added that the teratogenic effect of thalidomide is now thought to be accomplished through competitive inhibition of glutamic acid and glutamine.[46]

Exposure to infectious agents. If congenital malformations can be caused by viral agents, increased incidence of malformations following epidemics of viral diseases would be expected. Indeed, this was the way the teratogenicity of rubella was discovered and has been observed following the nationwide epidemic of rubella in the United States in 1964.[47] So far, however, no other teratogen has been identified by this approach, although one can suspect other maternal viral diseases may produce a variety of congenital heart defects in the child.[48–51]

DISCUSSION

Epidemiologic analysis of the distribution of a common disease with multiple etiologies is beset with many difficulties. Some of these have been mentioned in relation to the specific techniques as they were presented in the body of this paper. Others of more general importance will be mentioned below.

Epidemiologists have recognized for some time the fact that families not only share common genes but also share a common environment. A significant aggregation of disease in a family could therefore just as likely point toward an environmental influence as well as a genetic influence. Absence of increased incidence in two or more generations of a family points toward environmental effects predominating but does not rule out genetic effects, particularly in the context of a multifactorial etiology. Data reviewed under family aggregation studies is of interest but hardly conclusive in leading toward specific etiologic hypotheses.

Of even more fundamental concern is the problem of ascertainment. Most investigators now recognize the necessity of critical definition of congenital heart defects by objective criteria such as angiocardiography, heart catheterization, and so forth. Equally important is specificity of diagnosis, so that the epidemiologic patterns of the various types of aortic stenosis, for example, can be studied separately. To date, so many of the studies have treated all congenital heart defects as a single nosologic entity or, even, aortic stenosis as a specific defect having one specific cause, when all studies which have considered this question have concluded that these general categories include a number of significant subcategories which have to be studied individually.[52]

Embryologic studies of the heart have been a valuable tool in etiologic research of congenital defects of the cardiovascular system.[53] Significant contributions from the embryologist have included the following principles: [1] The earliest phases of heart development are under genetic control, but environmental influences appear to be more important in subsequent development. [2] Retarded development of cardiac anlage is generally due to environmental causes; incorrect anatomic positioning of the cardiac anlage is usually under genetic control.[54] These two hypotheses would lead to consideration of pulmonic and aortic valvular stenoses and transpositions of the aorta as primarily genetically determined

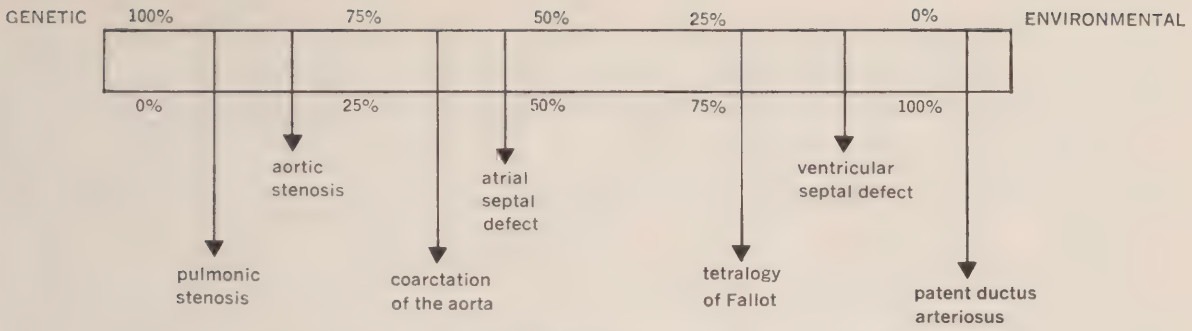


Fig. 1. The spectrum of congenital heart defects, with regard to the relative importance of genetic and environmental factors in etiology

defects and patent ductus arteriosus and atrial septal defect as primarily environmentally determined defects. This is in complete agreement with the epidemiologic studies reviewed in the body of the paper.

Unanswered questions are the rule and not the exception with studies of altered male:female incidence figures. As Potter[55] and others[56,57] have suggested, the malformations we see in children after birth are those compatible with intrauterine survival and actually may make up only a small proportion of the total number so affected. If this were so, this could be an explanation for the low incidence of familial aggregation of defects. An increased abortion rate usually indicates such a mechanism, however, and has not been reported in any series of cases.

The changing ratio of male:female cases through each successive decade, in the instance of atrial septal defects, dramatizes the problem of reliability of any such study based on hospital case records. Biases introduced by ascertaining cases only on the circumstances of attendance at a hospital can, of course, be significant and are not remedial by increasing the total number of cases ascertained. A prospective study utilizing the pregnancy and birth experiences of a carefully selected group of women would get around many of these objections but can become enormously complicated and time-consuming.

Another valuable method in studying etiologic factors in congenital heart disease, which has not been fully explored, is the classical twin study. Gedda and associates[58] have collected some interesting data in an attempt to look at the incidence of congenital heart lesions in twins in terms of specific defects, which represent a major improvement over pervious studies. Unfortunately, too few cases in each category have been collected to draw any meaningful conclusions. A study currently being conducted by the California State Department of Public Health is considering the incidence of congenital heart disease during the first year of life in all twins enrolled in the Twin Registry. This approach will hopefully remove many of the ascertainment biases of prior studies.

Where will all this lead? The answer to this question is neither simple nor obvious. Precise knowledge of etiology is, of course, always helpful, both in planning curative as well as preventive approaches to the disease in question. If the major congenital heart defects eventually prove to be multifactorially determined and all the genetic factors are not capable of being pinpointed, one still will be able to recognize and reshape the environment which is capable of precipitating a genetic inclination into an overt clinical disability.

The range of congenital cardiovascular defects constitutes a spectrum as to the relative importance of genetic and environmental factors in pathogenesis (Fig. 1). None are exclusively genetic, and few, if any, are wholly environmental. Toward one end of the spectrum are pulmonary valvular stenosis and aortic supravalvular stenosis. At the opposite end of the spectrum are the defects primarily determined by the environment. These would include patent ductus arteriosus and interventricular septal defect. Since most of the remaining conditions seem to be about equally determined by genetic and environmental factors, they can be considered midway between the two ends of the disease spectrum. This category includes tetralogy of Fallot, interatrial septal defects, and coarctation of the aorta.

SUMMARY

Congenital malformations of the cardiovascular system, taken separately, demonstrate a wide spectrum of genetic and environmental influences. On the one hand there are some defects, such as the incomplete atrial septum in the Holt-Oram syndrome, which have a clear-cut and relatively simple genetic basis. At the other extreme, there are some malformations, such as a

patent ductus arteriosus in the rubella syndrome, which show very little evidence of a genetic predisposition. However, the majority of congenital heart defects probably are caused by a combination of circumstances, involving many interacting genetic factors modified by a variety of nonspecific environmental influences.

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Changing Concepts of Pediatric Uroradiology

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EXAMINATIONS OF THE URINARY TRACT have become one of the most common and important procedures performed by pediatric radiologists. The increased interest in and demand for uroradiological procedures have been stimulated by 3 factors: (1) the high frequency of urinary tract infections in children, (2) insufficient knowledge of roentgenological pathophysiology and pathological anatomy, and (3) the development of radiological equipment conducive to examination of the urinary tract.

The increased interest in and concern for the urinary tract in children have naturally brought about many improvements and developments in uroradiological procedures, which in turn, have provided new information and knowledge of the anatomy and physiology. As a consequence, concepts considered valid ten years ago are no longer tenable, and new concepts are rapidly being replaced by new concepts in an area replete with misinformation and conflicting views.

The purpose of this paper is to mention and discuss, in a general way, some of these concepts which seem to be most basic and where change appears to be based on sound clinical information and investigation.

METHOD OF EXAMINATION OF THE URINARY TRACT

Some of the greatest changes have occurred in our concept of the proper method of examination of the urinary tract. This change is best reflected by tabulating the various radiological procedures performed in a year at a ten-year interval.

TABLE

Procedures	*Number of procedures per year* 1953	1963
Intravenous pelography	113	673
Cystourethrography	13	354
Retrograde pelography	128	9

The major factor responsible for the 6-fold increase in the number of intravenous pyelograms, as judged from the clinical records, is increased awareness of the relationship of urinary tract abnormality to fever of unknown origin, failure to thrive, abdominal pain, and genetic aberrations.

Several factors are responsible for the 27-fold increase in the number of cystourethrograms. One of these is developments in radiological equipment which have caused considerable change in the method of performing the examination. Formerly, a cystourethrogram usually consisted of a single film after the bladder was filled in a blind manner with an arbitrary amount of opaque material. The procedure was frequently performed on the cystoscopic table following cystoscopy in an anesthesized patient. Visualization of the bladder occurred only during the fraction of a second it took to expose the film, and the urethra and opaque material ran passively through it. Cystourethrography has now become a sophisticated examination, performed under image amplification and television fluoroscopy in a nonanesthesized patient, with multiple phototimed spot films, 16 mm. cine and 70 mm. spot films or both, providing excellent demonstration of the physiology and anatomy.

The meteoric rise of cystourethrography is also due to the widespread belief of radiologists and urologists that an evaluation of the urinary tract is incomplete without a cystourethrogram. In our practice, the cystourethrogram is a much more productive examination. It demonstrated pathology in 62% of 300 children with urinary tract infections, whereas the intravenous pyelogram was positive in only 36% of the same children. The two procedures, however, are not in competition but supplement each other. Each should be used in the examination of the urinary tract because together they yield positive information in 78% of the patients.

The decrease in retrograde pyelography is almost as dramatic as the increase in cystourethrography. The decrease is startling when it is realized that in 1953 retrograde pyelograms outnumbered the combined total of the other two. Improvements and refinements in the intravenous pyelogram and cystourethrogram have re-

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sulted in the indications for retrograde pyelography being limited to those instances where the collecting system, or a portion of it, is not visualized by intravenous pyelography and cystourethrography.

DILATION MEANS OBSTRUCTION

The idea that dilation of the calyces, pelves, and ureters means obstruction is deeply ingrained in medical thought and teaching. Obstruction causes dilation of the collecting system beyond a doubt, but that it is the sole cause, or even the most common cause, is being challenged by the frequent demonstration of hydronephrosis and hydroureter in the absence of obstruction (Fig. 1).

Instances of dilation of calyces, pelves, and ureters, in which it is difficult to find associated obstruction, are not new observations. In the past, such examples have either been considered as a wide variation of normal or diagnosed as poorly documented obstruction at some likely site. Casual observations and specific studies have shed some light on this problem.

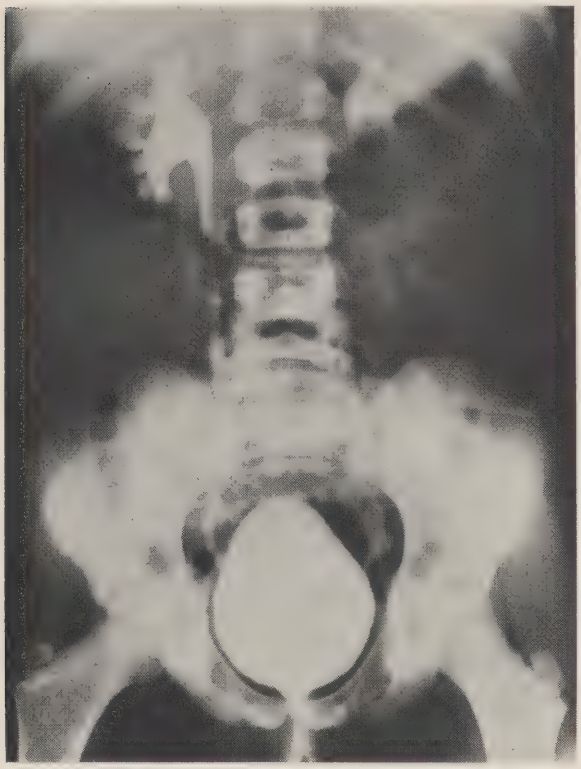


Fig. 1. Intravenous pyelogram in 7-year-old female admitted to hospital for urinary tract infection. Collecting system of right kidney shows dilation. Ureter is increased in diameter down to its entrance to bladder. Left kidney offers comparison with near-normal appearance. Complete diagnostic studies, including cystoscopy and cystourethrogram, revealed no obstruction. After appropriate treatment for infection, dilation disappeared.

Michie[1] believes that urinary infection damages the propulsive mechanism for urine flow; for example, the muscle in the pelvis, the infundibula, the ureters, and the bladder. The loss of muscle tone causes ineffective peristalsis and dilation.

Preliminary observations support Michie's contention that infection causes atony or ileus of the calyx, pelvis, and ureter.[2,3] One hundred twenty patients with collecting system dilation, but without obstruction, were examined by television fluoroscopy and appropriate documentary filming. Ninety-three had atony as indicated by sluggish peristalsis, persistent filling, segmentation, and back and forth swishing of the opaque material within the collecting system structures. All of these patients had infections of the urinary tract. Patients having intravenous pyelography, for reasons other than infection, were used as normal controls. Normally, the minor calyces receive opaque material from the papillary tubules in a continuous stream and remain filled much of the time. Periodically, the major calyces fill and then contract, expelling their contents into the renal pelvis. The renal pelvis, in turn, expels opaque material into the upper ureter which measures no more than 3 to 4 mm. in diameter, including magnification. Typical peristalic waves in the ureter pass the opacified urine quickly downward from one ureteral segment to another. This downward passage through the ureter is extremely fast and difficult to follow by fluoroscopy. There is no flabbiness, atonicity, or persistent filling of the normal ureter. Jonathan and Magri[4] observed the same phenomenon in their cine studies done in the evaluation of surgical treatment of ureteropelvic obstruction. They caution that the loss of musculature power and resultant delayed emptying should not be misconstrued as a continuation or recurrence of the obstruction at the ureteropelvic junction.

Others have observed collecting system dilation without obstruction but have concluded that it is due to reflux and refer to it as nonobstructive vesicoureteral reflux.[5,6] There is little doubt that reflux causes dilation (Fig. 2). In our group of 93 patients with infection and showing dilation without obstruction, only 52% exhibited vesicoureteral reflux. The greatest degrees of dilation were seen in those patients who had both atony and reflux.

The clinical observation that infection alone causes dilation was experimentally shown by Jeffs and Allen.[7] They established infection in 10 dogs without obstruction, and collecting system dilation occurred in 7, but reflux occurred in only 2. Nicolai[8] provides further evidence of

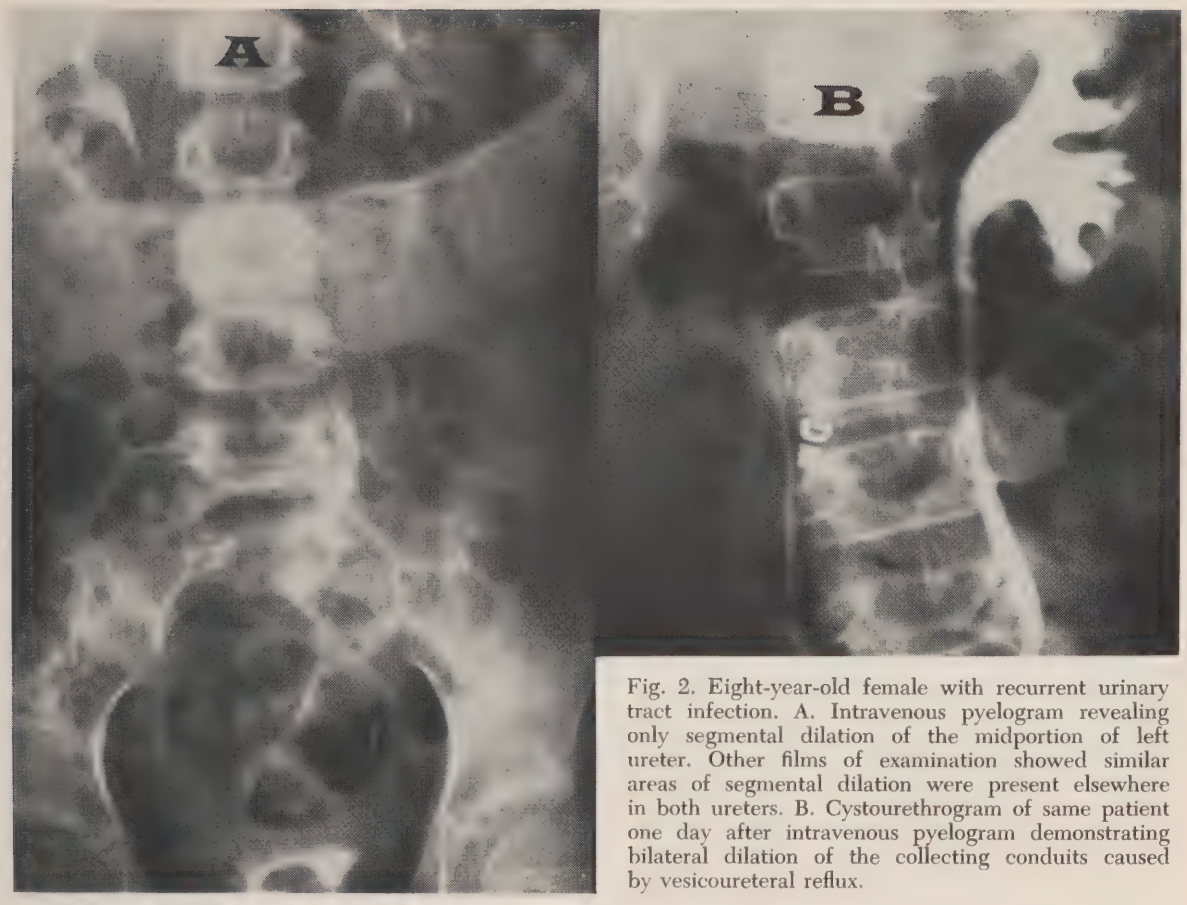


Fig. 2. Eight-year-old female with recurrent urinary tract infection. A. Intravenous pyelogram revealing only segmental dilation of the midportion of left ureter. Other films of examination showed similar areas of segmental dilation were present elsewhere in both ureters. B. Cystourethrogram of same patient one day after intravenous pyelogram demonstrating bilateral dilation of the collecting conduits caused by vesicoureteral reflux.

the dilating properties of pyelonephritis by showing that much greater hydronephrosis occurred in the infected kidney with a partially ligated ureter than did the noninfected controls.

In summary, dilation occurs without obstruction. The 2 offending agents are urinary infection and vesicoureteral reflux.

URETEROPELVIC JUNCTION OBSTRUCTION

The concept of ureteropelvic obstruction is undergoing considerable evolution. In 1953 a diagnosis of ureteropelvic junction obstruction was made 83 times in our department, and 74 operations for repair of ureteropelvic junction obstruction were performed in these patients. In 1963 the diagnosis of obstruction at this site was made only 5 times and there were 5 corrective operations performed.

During the period when the diagnosis of ureteropelvic junction obstruction was so popular, it was disturbing that there was difficulty in obtaining accurate surgical correlation of the roentgen findings. No obstruction could be found in some; in others, fibrous bands, anomalous vessels, and intrinsic ureteral stenosis were claimed to be causing the obstruction. Jonathan and Magri[4] have poignantly indicated that no abnormality was found in 35 of their 55 patients operated on for obstruction at the ureteropelvic junction.

An explanation for this apparent obstruction without an anatomical basis for it, was suggested in our study of the 120 patients who had hydronephrosis without evidence of obstruction.[3] There were features of the upper urinary tract which resembled ureteropelvic junction obstruction in 13 of the 120 patients (Fig. 3). In all instances in which the configuration of the renal pelvis, if taken alone, was typical of ureteropelvic junction obstruction, there was dilation and tortuosity of the ureters below the apparent obstruction.

It is an anatomical and physical fact that tubular structures, such as the ureters, become tortuous and kinked as they dilate. The ureters kink initially at the ureteropelvic and ureterovesical junction. Gross inspection at surgery and autopsy reveals that there are adhesions binding the walls of the ureter together at these points of kinking. In 2 children with pyelonephritis, we have observed intrinsic narrowing of the lumen of the ureter develop in a period of two years (Fig. 3).

It has already been shown that pyelonephritis causes dilation of the collecting system of the

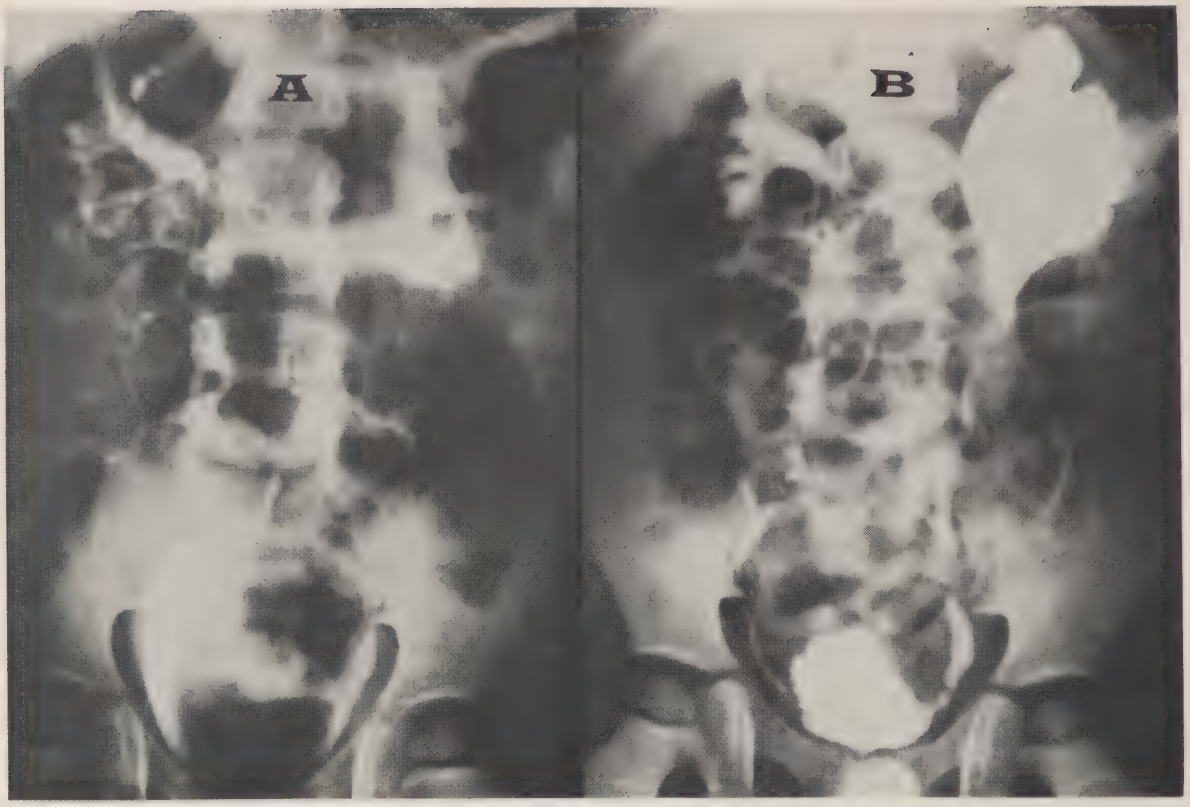


Fig. 3. A. Intravenous pyelogram in 5-year-old male after eighteen months of intermittent treatment for urinary tract infection. Pyelogram was previously normal but now shows dilation of left calyces and pelvis. This configuration alone is typical of ureteropelvic junction obstruction. However, note segmental dilation of lower third of left ureter. Fluoroscopy at this time demonstrated poor peristalsis, persistent filling, and segmental dilation of both ureters. B. Intravenous pyelogram six months after that shown in A. Dilation of left calyces and pelvis has progressed to an appearance characteristic of that ascribed to primary ureteropelvic junction obstruction, but note that entire left ureter is dilated and tortuous. Six more months of medical treatment resulted in some improvement. Surgical exploration demonstrated left ureteropelvic junction narrowing to be intrinsic stenosis.

kidneys, and vesicoureteral reflux accentuates and increases the degree of dilation with resultant tortuosity and kinking of the ureter. Ureteritis and periureteritis, which accompany pyelonephritis, cause adhesions and intrinsic stenosis at the site of the kinks where the walls of the ureters come to lie in an adjacent and parallel position. Hutch[6] has observed the same phenomenon but has attributed it to reflux. However, only 7 of the 13 patients in our study had reflux. Gondos[9] studied 24 patients with organic stenosis and adherent kinks of the ureters, 23 of whom had chronic lower tract infection. He concluded that ureteral stenosis and adherent kinks are most commonly the result of pyelonephritis, and their presence should be considered an indication of the presence of previous or current pyelonephritis.

The decrease in the diagnosis of ureteropelvic junction obstruction is due to the fact that the dilation of the renal pelvis and the ureteral kinking are recognized as signs of pyelonephritis. Proper medical treatment may result in the complete disappearance of the findings. The ureters returned to normal in 8 of the 13 patients in our study, and the signs of pelvic and ureteral dilation with ureteropelvic kinking improved significantly in the other 5. Extreme degrees of dilation are not reversible, and if chronic changes of intrinsic stenosis and periureteral adhesions are severe enough, secondary obstruction certainly does develop, but primary diagnosis and treatment should be directed at the basic cause. Treatment of the secondary ureteral obstruction should wait correction of the primary disease, either infection alone or with coexisting reflux.

These concepts of ureteropelvic junction obstruction can be applied equally well to ureterovesical junction obstruction ascribed to adhesions or stenosis.

URINARY TRACT INFECTION CAUSES REFLUX

Reflux customarily presents in patients with a past history of repeated bouts of urinary infec-

tion, although infection is not usually thought to be the cause of the condition. On the contrary, the opinion is prevalent that reflux causes infection.[5,6,10,11]

During the early period of evolving and maturing concepts of reflux, it was natural to think of it as being caused by urethral or bladder outlet obstruction. As recently as 1962 it was reported that reflux could not occur without abnormal pressure in the bladder.[12] Ross and Thompson,[13] while admitting that the hydrostatic pressures developed within the conduit system were inadequate to cause hydronephrosis, state that the patient with nonobstructive reflux may have an unrecognized obstruction. It has been firmly established that reflux occurs without evidence of obstruction.[5,6,10] In the reverse situation, proved urethral obstruction, the incidence of reflux is only 25%.

Anatomical investigations of reflux-permitting ureters show a shortening of the intravesical ureter, a patulous and laterally placed orifice, and scanty muscle replaced with fibrosis in the roof and side walls of the intravesical segment. The congenital theory for reflux, as an explanation for the anatomical findings, originated as naturally as the obstructive one. Hutch[14,15] believes there to be congenital immaturity of the intravesical ureter. Ambrose and Nicholson[16] postulated congenital lateral ureteral ectopia as one cause for reflux. The congenital theory leaves much to be desired because a perfectly normal urinary tract has been shown to start refluxing with the onset of infection, persist as long as there is infection, and disappear with the infection.

Hanley[17,18] may have been the first to officially suspect that infection causes reflux. Howerton and Lich[19] succinctly considered that reflux and urosepsis have an identical ratio in children, and reflux and infection in the bladder are inseparable. Jeffs and Allen[7] provided experimental evidence that bladder irritation and infection cause reflux.

Infection as a cause of reflux is explained by edema around the area of the trigone caused by ureteritis, cystitis, and urethritis, interfering with the delicate ureterovesical mechanism. It is not difficult or inconsistent to explain the pathological anatomy of the refluxing ureter on this basis. Chronic edema and inflammatory reaction could easily cause shortening, lateral ectopia, and fibrous scarring of the muscle of the intravesical ureter. Hanley[18] effectively provides clinical evidence for the infectious etiology of reflux by finding it in 25% of a group of women with only cystourethritis.

Doubt still exists that infection is the only cause of reflux because reflux occurs in patients in whom no infection is present at the time. In most such patients there will have been a history of previous infection. The presence of reflux in the face of negative cultures and urinalyses may be possibly explained on the basis of protoplasts.[20] Protoplasts, being bacteria without walls, require special culture techniques and are not detected by conventional methods. They appear to propagate the infection in a silent manner.

On the basis of current experience and information, vesicoureteral reflux is a manifestation of urethritis, cystitis, and ureteritis. Treatment for reflux should be primarily directed at eradication of the infection. Other forms of treatment, particularly surgical reconstruction of the ureterovesical junction, should not be considered until the effects of antibiotics and other drugs for infection have been determined. The presence of anatomical obstruction is not denied but it is usually secondary to infection. Eradication of the infection must be accomplished before it can be determined whether an anatomical abnormality exists.

BLADDER NECK OBSTRUCTION

The term "changing concepts" is nowhere more applicable than it is to bladder neck obstruction. This subject is confused by false impressions, veily assumptions, and emotionally based "truths" characteristic of teeming evolution.

Bladder neck obstruction has gained wide recognition because (1) back pressure initially seemed a logical explanation for ureteral reflux, (2) constrictions at the bladder neck are radiologically visible at the general area of the bladder neck, (3) cystoscopic evidence for bladder neck obstruction was easily obtainable, and (4) Wolgin,[21] Bodian,[22] and others provided anatomical basis for such obstruction.

The concept of bladder neck obstruction has become deeply rooted in spite of the fact that (1) its radiological and cystoscopic diagnosis was extremely variable, (2) little correlation of radiological and cystoscopic findings was possible,[3] surgical treatment results were questionable and seemed to be related to the presence or absence of infection, (4) reflux occurred without obstruction, and (5) good evidence that the findings being called bladder neck obstruction were in reality due to the detrusor muscle and were probably acquired and secondary.[23,24]

The basic tenet of bladder neck obstruction was destroyed when Lenaghan[25] reported that reflux was not correlated with high bladder pres-

sures or with urinary obstruction. The diagnosis of bladder neck obstruction is now so shaky that we have not made it during the past year. McGovern[26] is speaking the sentiments of a new breed of urologists when he says, "I do not think you can rely on endoscopy as a method of diagnosing bladder neck obstruction in children."

The constriction at the bladder neck, formerly misdiagnosed as bladder neck obstruction, is now known to be the detrusor muscle where it surrounds the urethrovesical junction (Fig. 4). Lapides,[27] in his excellent anatomical study, points out that the internal vesical sphincter is the true neck of the bladder, and that it is composed of the same type of mucosa, smooth muscle, and elastic tissue as the wall of the bladder. Uhlenhuth and Hunter,[28] and more recently Tanagho,[29] have shown that the trigonal muscle is a continuation of the ureter into the posterior urethra and is functionally and anatomically related to the bladder neck. The prominence of the constriction at the bladder neck is dependent upon the thickness of the detrusor muscle and the degree of filling, fullness, or dilation of the posterior urethra. Inflammatory spasm will also cause narrowing of the bladder neck (Fig. 5). A growing opinion[6,17,18] exists that primary bladder neck obstruction is not an entity and constrictions at the bladder neck are detrusor hypertrophy or inflammatory spasm.



Fig. 4. Cystourethrogram in 7-year-old male with recurrent urinary infection. Pyelonephritis is indicated by left vesicoureteral reflux, ureteral dilation, and segmentation. Narrowing at bladder neck (arrows) is caused by detrusor muscle hypertrophy secondary to cystitis. Meatal stenosis was cause of infection and meatotomy, plus treatment of the infection, resulted in disappearance of detrusor hypertrophy and reflux.

The demise of organic or anatomic bladder neck obstruction has left a void which is being partly filled by the concept of physiological bladder neck obstruction. Historical, radiological, and other clinical data does exist that voluntary retention leading to enlargement of the bladder, detrusor muscle hypertrophy, shortening and lateral displacement of the intravesical ureter, and ureteral reflux may result from infection.[1,18,22] Lapides'[26] opinion of the structure and function of the bladder neck lends support to the concept of physiological obstruction. Briefly, he states that the smooth muscle fibers of the bladder fundus and neck contract in a longitudinal fashion when micturation occurs. The contraction of the muscle fibers results in a widening or funneling at the vesical outlet. The contraction, not relaxation, of the smooth muscle results in a decrease in urethral length and tension, and an increase in the radius of the urethral lumen. The lowered urethral resistance and concomitant detrusor contraction allow voiding. Irritation, whether infectious, traumatic, or otherwise, can be logically expected to upset such an intricate mechanism.

We have clinically tested the traumatic role by taking 24 children with full bladders and placing them under exactly the same conditions we employ for cystourethrography. All 24 spontaneously voided and no significant residual urine was present before catheterization was performed for the cystourethrography which followed immediately. After the catheterization, 8 of the 24 children voided with difficulty, and 1 could not void at all. Recatheterization yielded significant residual urine varying from amounts of 25 cc. to 65 cc. The difficulty with urination and the residual urine following catheterization were due to dysuria and to reluctance of the pa-



Fig. 5. Urethrogram in 18-month-old male demonstrating inflammatory spasm of bladder neck and posterior urethra secondary to urethritis. Narrowing disappeared after three months of medical treatment.

tient to continue voiding once a degree of relief of the vesical distention was experienced.

Great restraint must be used in diagnosing bladder neck obstruction. Some basis for inflammatory stenosis and stricture at the bladder neck does exist, but consistency and persistency of the narrowing from such a lesion must be shown in 2 or 3 interval examinations following treatment of an infection (Fig. 5).

SUMMARY

1. Adequate radiological examination of the urinary tract in children should begin with cystourethrography and be followed by intravenous pyelography.

2. Retrograde pyelography is seldom indicated.

3. Dilation of the calyces, pelves, and ureters is most often due to infection, with or without associated reflux.

4. Ureteropelvic junction obstruction is most often secondary to infection. Treatment should first be directed at the infection because many apparent obstructions will disappear as the infection subsides.

5. Infection causes vesicoureteral reflux and treatment should be directed toward eradication of the infection before surgery at the ureterovesical junction is considered.

6. Bladder neck obstruction is exceedingly rare and radiological findings previously used to diagnose this condition are due to detrusor hypertrophy or inflammatory spasm.

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Hyperthyroidism, Hepatitis, Diabetes Mellitus, and a Myasthenia Gravis-Like Syndrome in a Seven-Year-Old Girl

DR. RILEY: We have a complex and interesting case to show you this morning, a 7-year-old girl who has several different medical problems. Dr. Cagas who has been following this patient closely will present the case. Drs. Smith and Jabbour plan to comment, but we will welcome any additional comments from the audience.

DR. CAGAS: This 7-year-old Negro girl was admitted to the Children's Memorial Hospital for the fifth time on August 6, 1964. She was first admitted in February 1963, with the chief complaint of "droopy eyelids" of six months' duration. The patient was well previously and had no other complaints. Physical examination at that time showed a well-developed, well-nourished Negro girl with ptosis and very poor extraocular muscle movements. The liver and spleen were enlarged three fingerbreadths below the costal margins. The thyroid gland was initially palpable, but not enlarged. There was no evidence of clinical hyperthyroidism. The liver function tests then revealed that the serum glutamic oxaloacetic transaminase (SGOT) was 917 units, and the albumin-globulin (A/G) ratio was reversed, being 3.4 gm. per 100 ml. albumin and 6.5 gm. per 100 ml. globulin. Subsequently, protein electrophoresis showed that the globulin fraction was mainly the gamma component. The twenty-four-hour radioiodine uptake was 40% (normal in our laboratory 15 to 40%) which remained at 39% after ten days of suppression with 75 μg. per day of triiodothyronine. The initial protein-bound iodine (PBI) was 13.3 μg. percent (normal 4 to 8 μg. percent). An intravenous edrophonium chloride (Tensilon® chloride) test produced a transient response in lid and extraocular muscle movements. The electromyogram was not diagnostic of myasthenia gravis, however, this was not ideal because patient cooperation was not obtained. The diagnosis then was possible myasthenia gravis. The child was treated with pyridostigmine bromide (Mestinon®), up to a maximum dose of 60 mg. every eight hours, but there was no response. Neostigmine (Prostigmin®) was then tried to the point of toxicity and there was a good initial response which lasted only three days. After that, there was no response. The child was readmitted in April, two months later, for further evaluation. At this time the liver and spleen were still enlarged. For the first time bilateral exophthalmos was noted. The exophthalmometric readings were 18 mm. in both eyes. The thyroid was now easily palpable and the PBI remained elevated. At this time, it was thought that the child had equivocal hyperthyroidism and she was started on propylthiouracil (PTU), 300 mg. per day, in divided doses. This was reduced to 200 mg. daily, three weeks later. The SGOT had come down to 400 units but the hypergammaglobulinemic pattern was maintained. Percutaneous liver biopsy showed round cell infiltration and minimal fibrosis tagged by the pathologist as "sub-

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acute hepatitis." Prostigmin® was discontinued for lack of effect.

Between the second and third admissions the child was followed in the outpatient clinic. During this interval of seven months the liver function tests were returning to normal. Although the thyroid gland was enlarging, with the neck circumference increasing from 25 cm. to 28 cm., the thyroid function tests were also returning to normal. Four months after the start of PTU therapy, PBI was 5.5 μg. percent and butanol-extractable iodine (BEI) 4.5 μg. percent (normal is 3.4 to 6.2 μg. percent). Thyroid antibodies by the tanned red-cell agglutination method were absent. Because the thyroid gland was still enlarging, despite an adequate propylthiouracil block, thyroid suppression with thyroid, 2 gr. per day, was started on January 2, 1964. The patient was readmitted on February 5, 1964 with jaundice and clinical hepatitis. Physical examination at that time showed moderate icterus and the liver and spleen had increased in size. However, the SGOT was only 327 units. Again, the reversed A/G ratio persisted.

DR. RILEY: Dr. Cagas, let me ask you what treatment she had been on immediately before the third admission.

DR. CAGAS: She was on PTU and desiccated thyroid. An intravenous cholangiogram at that time did not visualize the gallbladder. An intravenous Tensilon® chloride test conducted by the Pediatric Neurology Service was again described as dramatically positive. The thyroid profile was T-3 uptake (red-cell) 10.9% (normal 13.9%) and PBI 5.5 μg. percent. There was some concern about the PTU causing or aggravating the liver disease and it was discontinued. In June 1964, four months later, the child presented with polydipsia, polyuria, glycosuria without ketonuria, and a weight loss of 10 pounds over a two-month period. The clinical picture was that of diabetes mellitus. The initial insulin requirement was 45 units per day. The thyroid profile showed a T-3 uptake that had increased to 28.6% and a radioiodine (RAI) uptake of 28%, in twenty-four hours. There is a discrepancy here, because a T-3 uptake of 28.6% is in the hyperthyroid range while an RAI uptake of 28% is normal. However, it is possible this is falsely elevated because of the recent intravenous administration of iopanoic acid (Telepaque®). A PBI was not obtained because of the recent cholangiogram. The liver function tests had returned to normal except for persistent hyperglobulinemia. In a subsequent clinic visit six weeks ago, the child was observed to have a right seventh nerve palsy of the central type. At this time, Mestinon®, 30 mg. every four hours, was tried and again there was no response. During this clinic visit, it was thought that the patient was borderline normal and borderline hyperthyroid, the only sign of the latter being persistent resting tachycardia. It was decided to increase the thyroid medication to 3 gr. for one week. There was no clinical change. However, the mother told us at this point that the child was somewhat more restless in her sleep, and although sleeping pulses were not counted, the mother thought that they were rapid. Subsequently, the sleeping pulses in the hospital were mostly between 110 and 120 per minute, but there were recordings below 95. At the time of the fifth and present admission, the thyroid gland was very firm and lobular and enlarged three to four times its usual size. The liver was no longer enlarged but the spleen was still enlarged to 7 cm. An intravenous Tensilon chloride® test done at this time was considered positive but the response was not as dramatic as previously observed (Figs. 1 and 2). Since this admission, the patient's insulin requirement has almost doubled, from 48 to 85 units.

Laboratory data during this admission include: serum thyroxine and T-3 uptake (Bioscience, California), two days after the desiccated thyroid was stopped, 11 μg. percent and 17.1%, respectively. These are both elevated.

The twenty-four-hour thyroid radioiodine uptake, obtained four days after thyroid was stopped, was 63% and a basal metabolic rate test (BMR) done four weeks after the medication was stopped was +33. The microscopic picture of the thyroid obtained from a small open biopsy showed some giant cells, areas with granulomatous changes without fibrosis, and some hyperplastic follicles. This was thought to represent follicular hyperplasia and granulomatous giant cell thyroiditis. Biopsy of a small epitrochlear lymph node was nondiagnostic. The child was studied from an autoimmune aspect, as she had been in the past, to include VDRL, Coombs' test, lupus erythematosus (L.E.) cell preparations, and latex fixation test, but all studies were negative. Again there were no thyroid antibodies detectable by the tanned red-cell agglutination method. The histoplasmin and tuberculin skin tests done in the past and also on this admission were also negative.

In summary, this is a 7-year-old Negro girl who presented with the following clinical features: [1] a myasthenia gravis-like picture, characterized by ptosis, complete ophthalmoplegia, and seventh nerve palsy. It is of interest that



Fig. 1. Control (before Tensilon® test), note bilateral ptosis and exophthalmos.



Fig. 2. Note improvement of the ptosis and the residual right-sided seventh nerve palsy one minute after the intravenous Tensilon® test.

when the child wakes up the eyes are wide open. Only the other day I saw this child just awakened from sleep and she did move her eyeballs. I should hasten to add also that the myasthenia gravis picture has been refractory to Prostigmin® and Mestinon®. [2] Thyroid disease, consisting of a clinical picture in keeping with mild hyperthyroidism, convincing laboratory data of definite hyperthyroidism, and a histological picture of giant cell thyroiditis and follicular hyperplasia is present. [3] Hepatosplenomegaly has been noted. The nature of the splenic enlargement is unknown but we know that the liver biopsy showed subacute hepatitis. The SGOT was elevated to 1,000 units at the most; the liver function tests have since returned to normal levels. The spleen is still enlarged but the liver is no longer palpable. [4] Diabetes mellitus, characterized by an initial insulin requirement of 45 units nearly doubled since admission and by the absence of ketonuria in the presence of severe glycosuria, completes the list.

DR. BUCHNER: May I ask how high the blood sugar has been?

DR. CAGAS: The blood sugar has been very high; initially, when she presented with polydipsia, polyuria, and weight loss, fasting blood sugar was 490 mg. percent.

DR. RILEY: Do you want to see the patient now or do you want to show the slides or photographs that you mentioned? While she is coming in, let me introduce to the group Dr. Joseph Foley, who is professor of neurology at Western Reserve University. Dr. Foley, we will be happy for you to help us in any way that you can.

DR. FOLEY: Don't get your hopes up too high.

DR. CAGAS: This is the thyroid, and this is a scar of the thyroid biopsy. We think that since the thyroid biopsy, the thyroid gland has become smaller. Perhaps the biopsy had some therapeutic effect. (Laughter)

DR. FOLEY: More than you think.

DR. CAGAS: Have you any questions, or do you want to see her now?

DR. JABBOUR: Tap her reflexes—she has always had rather hyperactive reflexes and from time to time they become quite brisk, but she doesn't have a Babinski or clonus.

DR. FOLEY: Could I ask Dr. Cagas if her ptosis increases on upward gaze or does it remain fixed?

DR. CAGAS: The ptosis is always fixed, as it is now.

DR. FOLEY: You can't make it worse than it is now?

DR. CAGAS: No.

DR. FOLEY: Get her to wrinkle her brow, if she can.

DR. CAGAS: Wrinkle your brow, Naomi, please.

DR. JABBOUR: Smile real big, Naomi. How do you feel this morning?

DR. FOLEY: Dr. Cagas, can she close her eyes tight?

DR. CAGAS: Naomi, will you close your eyes for us, please? Real tight, come on, real tight. See the strength on the right side! This is the reason why we thought it was the central type of seventh nerve palsy which has improved since then. Thank you, Naomi. I will see you later.

I am now going to show the pictures we have of this patient. The first picture shows the patient one year before the onset of symptoms. Notice there is some semblance of ptosis on the right side. The next picture shows the thyroid enlargement and ptosis. The next picture is a close-up of the ptosis before the most recent Tensilon chloride® test (Fig. 1). The following picture shows the results of the Tensilon® chloride test

(Fig. 2). Note that the eyelids were lifted up. Possibly there might have been some eyeball movements at the time which were not caught by the camera. The same picture shows the facial asymmetry sustained during the Tensilon test. She still had some right-sided palsy there.

DR. BUCHNER: Has this girl received any cobalt preparation?

DR. CAGAS: No.

DR. RILEY: Are there any other questions for Dr. Cagas?

DR. SEELY: I think, Dr. Cagas, there was some evaluation of adrenal function.

DR. JABBOUR: Is there any pertinent family history, Dr. Cagas?

DR. CAGAS: Yes, Dr. Jabbour. We found that the father presently has multiple sclerosis and diffuse nontoxic goiter. There have been no goiter studies because the interest was mainly on the multiple sclerosis angle. The adrenal study that Dr. Seely referred to was a normal urinary corticoid response to metyrapone (Metopirone®) which would indicate an intact pituitary-adrenal axis.

DR. KIRKMAN: Does anyone else in the family have ptosis?

DR. CAGAS: No. There is no family history of liver disease, diabetes mellitus, or myasthenia gravis.

DR. RILEY: Are there any other questions for Dr. Cagas? Dr. Smith.

DR. SMITH: I previously have had the pleasure of discussing the problem of simple goiters in childhood at these Staff Rounds. Today, the discussion centers about a child with multiple problems, one of which is an unusual thyroid disorder that is far from simple. One's first impulse is to ascribe these multiple system dysfunctions to an autoimmune phenomenon involving the various organs, perhaps initiated through an alteration in the reticuloendothelial system. This unitary explanation for this child's many problems has provoked considerable skepticism from my colleagues and, admittedly, at this point, we have demonstrated no significant evidence for its support. Nevertheless, I still feel this is an area that warrants a brief review of some of the suspected, if not proven, associations with multiple organ system disorders.

While not deliberately ignoring the chronology of this child's problems, Dr. Jabbour and his neurological colleagues will be our clean-up batters and discuss the relationship of myasthenia gravis to other disorders at the end of the conference.

In attempting to tie these various disorders together, one can immediately think of associations of thyroid disease and diabetes mellitus. Liver disease in diabetes mellitus has been reported and, in fact, I have seen 2 children with the onset of diabetes initiated or heralded by what seemed to be acute hepatitis. We know that in diabetics and, specifically but not exclusively juvenile diabetics, the incidence of circulating thyroglobulin antibodies is around 22%, whereas in the normal population it runs between 5 and 8%. This finding would give some support to the idea that something is occurring on an autoimmune basis in these children. Looking further, we know that in the various connective tissue diseases there is an increased incidence of lymphocytic thyroiditis and in these disorders without obvious thyroid disease there is an increased incidence of circulating thyroid antibodies.

The initial understanding or at least the concept of autoimmune endocrinopathies began about eight years ago with the discovery that thyroiditis could be produced in rabbits by immunizing them against thyroid tissue. Also, circulating thyroid antibodies that can be identified by several techniques are present in high concentrations in individuals with lymphocytic thyroiditis. Initially, it was felt that the circulating antibodies somehow damaged the thyroid and produced a thyroiditis. However, so far, clinical and experimental studies tend to indicate that the circulating antibodies are not the etiologic agents but that autoimmune thyroid disease is probably a manifestation of a delayed rather than an immediate hypersensitization. The finding of high antibody titers in 20% of cases of spontaneous myxedema led to the idea that this disease in many instances is the result of complete destruction of the thyroid by an autoimmune process. Last year, in my discussion of Hashimoto's thyroiditis in children, I presented a case of acquired myxedema in an 8-year-old boy that tends to confirm this concept. Thyroid antibody titers were very high and biopsy of the atrophic gland showed almost complete replacement of the follicles by classic lymphoid proliferation. Still unexplained is how or why this process begins. Cases of familial lymphocytic thyroiditis and the finding of thyroid antibodies in 50% of relatives of patients with Hashimoto's disease strongly suggest a genetic predisposition. This still fails to explain how or why the process begins. An unknown factor or agent, perhaps infectious, may initiate release of thyroid antigens from the gland, thus beginning the sensitization process.

It was logical to extend this general concept to diseases of other endocrine glands. Attention

was especially directed toward idiopathic Addison's disease, since this may represent the counterpart of spontaneous myxedema. Blizzard and associates found adrenal antibodies in the sera of 53% of 30 patients with Addison's disease; 7 had, in addition, coincidental thyroid antibodies. Experimental autoimmune adrenalitis has been produced in rabbits and guinea pigs, but the specificity of the lesion has been questioned. In the same vein, the rather frequent association of hypoparathyroidism and hypoadrenalism and, in some instances, superficial moniliasis has suggested an autoimmune mechanism. Familial instances of this triad have occurred. The simultaneous occurrence of Addison's disease, diabetes mellitus, and thyroid disease has been reported. Furthermore, two cases of diabetes mellitus with primary thyroid, adrenal, and gonadal insufficiency have been documented. At any rate, we are beginning to see that a variety of endocrine deficiencies can occur in the same patient. If these multiple endocrine deficiencies do in fact represent manifestations of an autoimmune process as pointed out by Solomon and Blizzard,[1] the occurrence of multiple antigen-antibody complexes implies an underlying abnormality in the reticuloendothelial system.

We might mention again that this child has no apparent genetic predisposition for her multiple endocrine disorders. However, the familial occurrence of many of these apparently autoimmune endocrine diseases strongly suggests that undetermined genetic factors have a role in their etiology.

A logical and frequently asked question about this child is, why is the myasthenia and diabetes not wholly explained on the basis of thyrotoxicosis? The relationship of thyrotoxicosis and myasthenia will be discussed later by Dr. Jabbour and Dr. Cagas. Admittedly, diabetes mellitus could be difficult to diagnose in a child with thyrotoxicosis. It is well known that the intestinal effect on carbohydrate metabolism results in about one-third or more thyrotoxic patients having hyperglycemia and glycosuria some time in the course of their disease. However, there is no correlation between the severity of the thyrotoxicosis and the degree of carbohydrate intolerance. Approximately 70% of the patients that have had hyperglycemia or glycosuria will return to a normal carbohydrate state after treatment of the thyrotoxicosis, while in the other 30% the hyperglycemia persists. The combination of diseases occurred in 1% of diabetics in 1 large series while among some 20,000 patients with hyperthyroidism in another series, 2.3% were diabetic.[2] There is not a breakdown of the relative incidence in juvenile diabetes or juvenile thyrotoxicosis.

In this child, the diagnosis of diabetes mellitus is strongly supported by the explosive clinical picture of polydipsia, polyuria, weight loss, hyperglycemia, and glycosuria without an obvious exaggeration of the hypermetabolic state which responded promptly to insulin administration. I would like to point out that we have no explanation as to why this child developed such a sudden, severe diabetic state without ketosis. She had only a trace of urine acetone on admission to the hospital in June and none since. This is somewhat unexpected in juvenile diabetes and we have found no evidence that diabetes occurring with thyrotoxicosis is characterized by an absence of ketosis such as happens with steroid diabetes.

The 2 striking clinical features of this child's thyroid disease that have caused considerable concern and confusion to most observers are the relatively few overt signs of thyrotoxicity and the hard, almost woody consistency of the gland. The proptosis has progressed gradually with measurements increasing from 18 to 21 mm. in each eye, but there is some question as to whether the exophoria has accentuated the measurements. The persistent tachycardia is the only other sign of thyrotoxicosis that has been impressive. This child is not at all hyperactive or emotionally labile or nervous. She has no weakness of the extremities or trunk. Some have thought her skin was unusually smooth, soft, and thin, however, the mother and the younger sister have nice, smooth, soft skin. In fact, this child is somewhat similar to 2 children I have seen with so-called apathetic thyrotoxicosis which is more frequently seen in adults. Apparently, some adults with this type of disease may develop severe thyrotoxic crises or cardiac failure without manifesting any other significant signs of the disease.

The extreme firmness of the gland may be explained by the unexpected biopsy findings of giant cell granulomatous thyroiditis in addition to areas of follicular hyperplasia. Giant cell thyroiditis is a relatively rare disease and has not been reported in children under age 18 or 19 in the case reports that we have been able to review. The incidence of granulomatous thyroiditis in approximately 42,000 thyroid operations reported from Mayo Clinic was 0.26%.[2] Granulomatous thyroiditis classically starts with pain and tenderness in the neck and is often associated with an upper respiratory infection. It does not become suppurative and the goiters are described as small and very hard. Again, we

have been impressed by the extreme firmness of this gland which is quite unlike that we expect in Hashimoto's thyroiditis or thyrotoxicosis. Cellular hyperplasia has been found with giant cell thyroiditis but this has been interpreted as an effort at compensation in the late stages of the disease. It was suggested that some of the patients may have gone through a transient phase of thyrotoxicosis such as may occur with lymphocytic thyroiditis, but this was not documented adequately by clinical or thyroid function studies. It has been postulated that granulomatous giant cell thyroiditis like lymphocytic thyroiditis is also due to autoimmune disease, but there are no antibody studies reported to lend support to this possibility. In this child, thyroid antibodies measured on 2 occasions by the tanned red-cell hemagglutination technique have shown insignificant titers. However, approximately 25% of proven cases of lymphocytic thyroiditis do not have positive tests by this method. Therefore, it would be necessary to use a battery of tests, such as complement fixation, precipitin, Coombs' technique on thyroid section, and tissue culture methods to be sure thyroid antibodies are not present.

Finally, a brief word about the past and proposed management of these multiple problems. Management of the diabetes has posed no particular problem other than a heavy spill of urine sugar without acetone that persists even with increasing insulin doses of up to 88 units NPH insulin per day. The measurement of insulin antibodies before administration of insulin would have been of considerable importance in establishing this multiple endocrine disorder as an autoimmune phenomenon. Insulin antibodies may still be a factor in the increasing insulin requirements.

Fortunately, at present, the liver function studies are normal and, hopefully, the hepatitis is in complete remission. It should be mentioned that liver involvement with thyrotoxicosis is well known. However, many of the best known earlier reports of postmortem studies describing "thyroid cirrhosis" were made before antithyroid drugs were widely used and before the multiple debilitating factors were rapidly corrected. In fact, later studies have shown few changes in most instances other than glycogen depletion even in patients dying in thyroid crisis. Nevertheless, this child seems to have had true hepatitis and whether or not it was related to the thyrotoxicosis and perhaps exacerbated by the propylthiouracil therapy is still debatable.

The major problem in management at this time is the thyrotoxicosis. Although there was a return to normal of the PBI and thyroid I^{131} uptake while on propylthiouracil, there was no clinical change other than the progressive enlargement of the goiter, possibly an increase in the exophthalmos, and, as mentioned, possibly an associated exacerbation of the hepatitis to produce overt jaundice. Because of this latter problem, I doubt if any of us would risk another course of therapy with thiouracil drugs even in preparation for surgery. There is somewhat the same concern in initiating therapy with potassium perchlorate. Despite the increased risks of neoplasia and genetic alteration following administration of radioiodine to children, this form of therapy is seriously being considered for this child. In all but a few medical centers there are enough complications from thyroidectomies in juvenile thyrotoxicosis, without the additional hazards imposed on this child, to make most pediatric endocrinologists prefer some form of medical therapy. Fortunately, this child's thyrotoxicosis is mild and we do not feel forced to make a decision immediately without further consultations.

DR. RILEY: Dr. Jabbour, will you comment?

DR. JABBOUR: I will limit my discussion to a few points found in a review of the literature and the relationship of hyperthyroidism to myasthenia gravis.

This child initially was diagnosed as myasthenia gravis, but as the problem evolved we realized that the endocrinologist might help us relate the entire problem to one disorder.

Although this interesting disease was first described in 1672, it was further delineated in the late eighteen hundreds. Teng[3] and Millichap[4] have recently reviewed myasthenia gravis in children. Over 200 cases were documented by 1956 and since then the literature contains almost twice this number of instances in both children and adults. Most patients had signs of the disease very early and a large number were noted at birth or immediately thereafter.

The classification of myasthenia gravis differs very little from author to author. Congenital transient myasthenia gravis occurs in the infants of mothers with myasthenia gravis. The infants respond to minimal doses of Prostigmin® and usually become free of signs over a period of one to twelve weeks. Transient myasthenia gravis is recorded in approximately 10% of mothers who have myasthenia gravis. Teng[3] classifies the disorder as transient and juvenile myasthenia gravis. Many of the subjects have an initial problem with weakness of the cranial nerves and several of the patients recorded, similar to the child presented today, had predominantly bilateral exter-

nal ophthalmoplegia. Millichap[4] introduced the term, "congenital persistent myasthenia gravis," which begins after birth, usually by 3 years of age. The most interesting group of cases in these 2 series of 250 were 25 patients with predominant signs and symptoms related to cranial nerve palsies, especially those of the eyes. In these cases there were several familial instances in cousins or sisters. I should also point out that the ratio of female to male was high, approximately 6:1, and this has been previously recorded.

The most disturbing factor in these patients we have been following as well as those described in the literature has been the minimal response to Prostigmin® and difficulty in determining the progression of the disease. In some subjects the disease has progressed rapidly while others deteriorate slowly. Another observation which has been helpful in determining the prognosis in these patients relates to the areas of muscular involvement. If myasthenia gravis remains localized to the eye muscles for three years it will usually be a disease of limited involvement.

What about the relationship of hyperthyroidism to myasthenia gravis? We were initially impressed with the laboratory confirmation of hyperthyroidism and thought that with treatment this child's signs of the disorder would partially disappear. Now I feel that our initial impression of myasthenia gravis must be considered again.

Dr. Buchner was the attending physician on the ward to which this child was admitted and suggested that she had exophthalmos and should have a thyroid evaluation.

The relationship of hyperthyroidism and myasthenia gravis was recently reviewed by Greenberg[5] in 2 sisters. The initial impression was that 5 to 6% of patients with myasthenia gravis would develop hyperthyroidism. Conversely, only 1% of patients with hyperthyroidism seem to develop myasthenia gravis. The most interesting feature of the relationship was the seesaw effect. This was observed in several cases. As the hyperthyroidism increased in severity, the signs and symptoms of myasthenia gravis seemed to regress. When the hyperthyroidism was treated the myasthenia gravis became worse. Since this initial observation several reports have not confirmed this impression.

Hereditary factors in myasthenia gravis and hyperthyroidism have been studied extensively. Several instances of myasthenia gravis have been recorded in siblings within 1 large family. The disorder may occur in mother and child or in family members or it may be observed in several generations. Nearly 20 pedigrees with familial myasthenia gravis have been documented in the literature.

The factors of heredity in hyperthyroidism have been reviewed by Martin and Fisher. A recessive mode of inheritance with possible sex-linked factors seems likely. Thus, the complexity of the present case and those previously recorded in the literature make us realize that myasthenia gravis is an expression of disease resulting from multiple organ involvement and further studies in all cases should be performed. Only in this way can the pathophysiologic interrelation of neuromuscular function in other organs be determined.

DR. RILEY: Dr. Cagas has also reviewed this subject recently and will make additional comments at this time.

DR. CAGAS: One of the questions which we have not quite satisfactorily answered in this patient concerns the nature of the profound ophthalmoplegia. Does it represent true myasthenia gravis, or is it part and parcel of hyperthyroidism—chronic thyrotoxic myopathy? The differentiation of myasthenia gravis with coexistent hyperthyroidism from chronic thyrotoxic myopathy can be hair splitting, especially if the presenting symptom is ophthalmoplegia only. I therefore doubt the wisdom of making a distinction between the 2 in a most formidable case such as this. I shall, however, attempt to face the present dilemma in the light of available literature.

For many years, faradic stimulation used to be the only diagnostic tool for myasthenia gravis, until 1934 when the advent of Prostigmin® marked a new era in the diagnosis and treatment of this disorder. Subsequently the introduction of other tests such as the use of d-tubocurarine helped the clinician to differentiate myasthenia gravis from other forms of neuromuscular diseases. Danowski[6] tabulated the points of difference between the two conditions. The involvement of cranial nerves other than or in addition to the third, fourth and sixth, improvement with neostigmine or related drugs, and sensitivity to d-tubocurarine are taken as positive evidence for the presence of myasthenia gravis while the converse, plus the finding of muscle wasting and favorable response to antithyroid therapy are considered good evidence for the other.

Unfortunately, our patient presents with unusual and atypical features. On the basis of the aforementioned criteria, the following points may be considered evidence for the presence of myasthenia gravis: involvement of the seventh nerve in addition to the third, fourth and sixth, a positive response to Tensilon® chloride, and

an initially good, although transient, response to Prostigmin®. The fact that the ptosis and extraocular muscles improve immediately after awaking and that the patient is a female are additional arguments in favor of myasthenia gravis. The only valid argument against this diagnosis is her refractoriness to Prostigmin® and Mestinon® therapy. The presence of exophthalmos can not be interpreted as proof of thyrotoxic myopathy for it has been known to occur in myasthenia gravis even in the absence of hyperthyroidism. The fact that this patient does not present a clear-cut picture, in itself, may be regarded as further evidence of the interesting combination. Lastly, the additional diagnosis of myasthenia gravis in this patient fits very well into the autoimmune hypothesis as discussed earlier by Dr. Smith, this condition being known to be associated with thymic abnormalities, other diseases, and certain conditions considered to be autoimmune in nature.

The great majority of patients with myasthenia gravis and thyroid disease have been hyperthyroid, although a few patients with hypothyroidism have been reported. In view of the autoimmune implication, it is very surprising that only 2 instances of clinical Hashimoto's thyroiditis and myasthenia gravis are recorded in the literature.[5] Becker and associates[7] recently, however, found at autopsy 6 cases of Hashimoto's thyroiditis among 32 cases of fatal myasthenia gravis. The first probable case of coexistent myasthenia gravis and hyperthyroidism was reported in 1908 and the first well-documented case in the American literature in 1928. Three years ago, Engel[8] collected 93 cases in the literature. Of the 75 patients in whom sex was identified, 61 were women. The incidence of hyperthyroidism in patients with myasthenia gravis varies from 3 to 8.8%. The 5% figure quoted by Dr. Jabbour from the Mayo Clinic group[9] is probably representative. Although cases in childhood had been reported in the German literature, the vast majority of the patients reported with this combination of diseases were between 20 and 60 years of age. Hyperthyroidism can develop at any time with respect to the onset of myasthenia gravis. Of the 25 cases reviewed by Millikan and Haines,[9] 36% developed hyperthyroidism first, 32% had myasthenia gravis first, and in only 9% did the 2 diseases begin simultaneously. In the cases reviewed by Engel,[8] the mean age of onset of hyperthyroidism was 32.8 years and the corresponding figure for myasthenia gravis was 34.4. The mortality rate was 30.1%.

In summary, it appears that there is no clear-cut criteria distinguishing true myasthenia gravis plus hyperthyroidism from chronic thyrotoxic myopathy. If one accepts the criteria as tabulated by Danowski,[6] it would appear that the coexistence of myasthenia gravis and hyperthyroidism is not a rarity except in the pediatric age group. The fact that the patient presented today does not exhibit a true myasthenia gravis picture may be interpreted as evidence of the occurrence of this syndrome.

DR. RILEY: We might ask Dr. Foley if he has any comments on this or if he has seen this combination.

DR. FOLEY: No. If I do, I will send it down. This sort of case is one that could take up a man's entire time. I would dissent completely, of course, on the diagnosis of myasthenia gravis. I don't think she has it. I think that she has a myopathy of the ocular muscles, probably related to the rest of her general disease. This degree of response to Tensilon® chloride you can get with polymyositis, you can get it with dystrophy of the ocular muscles, and unless you get a complete reversal in the first few seconds after the Tensilon® chloride, it is unwise to call the test positive. The other thing that strikes me is that in the presence of such profound involvement of the extraocular muscles, she has, it seems to me, surprisingly good strength of the orbicularis oculi. When the levator is involved in myasthenia gravis, inevitably the orbicularis oculi is involved. There are some interesting angles about this case, however. I wonder if it might not be worthwhile to get a muscle biopsy from somewhere around the shoulder girdle to see if you can elicit any evidence of myopathy there. It well may be that this is the kind of myopathy that affects not only skeletal but also cardiac muscle. She might well have a cardiomyopathy in conjunction with the skeletal muscle myopathy and this might be the basis for her tachycardia. I would also like to know something about her father's multiple sclerosis. The old gentleman ought to be looked at carefully. One interesting point about malignancy, in relation to myasthenia gravis, was brought home to me again forcefully within the past week when a man came in with myasthenia gravis involving everything except his ocular muscles. These were his only normal muscles and on this basis alone we concluded that he had bronchogenic carcinoma. Whenever you see myasthenia gravis that responds beautifully to Tensilon® chloride and poorly to neostigmine, then you can be almost certain, in the absence of extraocular muscle involvement, that you are dealing with a malignant disease.

DR. RILEY: Dr. Jabbour, am I correct in saying

that right after her first admission you and others felt pretty definitely she had myasthenia gravis, but in the next few months, or at least when she was readmitted, this diagnosis was then questioned?

DR. JABBOUR: Initially, I think that her response was as Dr. Foley described. It was a more dramatic response. We have 2 or 3 other patients whom we are following, with what we are calling myasthenia gravis, but who may have muscular dystrophy of the eyeballs or other myopathies. However, they too have manifested progressive disease and have not reacted as dramatically to Tensilon® chloride as the patient presented today. It is interesting also that from time to time, in the late evening, this girl has been noted to have difficulty in drinking water and eating. We wonder if there isn't some involvement in other muscles. I wonder, also, about the relationship of the seventh nerve weakness which I believe is really more peripheral. The other patients with myasthenia gravis in our clinic had a minimal seventh nerve involvement.

DR. RILEY: Dr. Buchner, do you have any comments since you have seen this patient on the ward?

DR. BUCHNER: No, except that I am surprised to see the size of her thyroid gland. There has been a striking increase in the size. Also, she always struck me as having a very mild exophthalmos and I think now she has a little bit more than she had when I first saw her. As far as myasthenia gravis is concerned, we were not really impressed with our therapy.

DR. RILEY: We are about out of time, and I think we should close. Are there any final comments from any of the speakers or the audience?

Thank you.

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Robert Emmett Farr
1875-1932

STANLEY R. MAXEINER, M.D.
Minneapolis



ROBERT EMMETT FARR was born at Montello, Wis., Feb. 15, 1875. His parents were both Irish and devout Roman Catholics. He attended school in Milwaukee and after graduation entered Rush Medical College in Chicago where he received his M.D. He was extremely vigorous and athletic and played football as a medical student on the Rush Medical team, of which he was captain. During his early years of practice he served as football coach at Macalester College.

As a student and intern at St. Mary's Hospital in Minneapolis, he became acquainted with a famous staff surgeon, Dr. James Dunn. After his intern service he became assistant and partner of Dr. Dunn, which continued until Dr. Dunn's untimely and sudden death during or immediately after giving an address before the American Medical Association at St. Louis. Dr. Farr held Dr. Dunn in very high esteem which, undoubtedly, greatly influenced his ideals and teachings.

Dr. Farr was on the teaching staff at the University of Minnesota from 1902-1914. He also served on the surgical staff of the now Hennepin County General Hospital. It was there, as an intern, that I served on the service of Dr. Farr and later became his assistant and partner, which extended over a period of about twelve years.

Dr. Farr was never satisfied with a status quo, which was undoubtedly a factor in his constant search for new and better methods of surgery. I recall during the typhoid epidemic in 1909-1910, while on his service at the then City Hospital, he attended a severely comminuted leg fracture on a typhoid patient with wild delirium. He performed skeletal traction by means of a carpenter's nail through the os calcis, which maintained perfect position of the fragments inspite of the patient's tossing about. He was probably the first patient treated with skeletal traction in this area, and for which Dr. Farr was severely criticized for using a new, unaccepted, pioneering procedure. Searching for advancement and improvement seemed to be a characteristic of his. He was one of the early workers with X-ray machines; first the static turned with a hand crank, later with the chemical and mercury interrupters, and finally with the present type. He often told of turning the crank on the static machine for ten or fifteen minutes for a kidney exposure and found he had forgotten to put the glass plate under the patient.

During the early years of his practice, anyone handy—usually an inexperienced intern or a nurse—gave anesthetics. A very cyanotic patient or one who temporarily stopped breathing was a too-frequent experience. These happenings prompted his adoption of local anesthesia. Cocaine and novocain were the drugs employed. To perfect their use he researched these drugs for their toxicity and efficiency. Novocain, with or

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without adrenalin, was accepted for most procedures. Dr. Farr was one of the first surgeons to use music in his operating room. Many hours were spent in the autopsy room and in the library in a study of the afferent nerves of viscera and skeletal tissues. He constantly taught the importance of nontraumatic handling of tissues.

He became a prolific writer on local anesthesia which accounted largely for his national and international reputation. His operating room at St. Mary's Hospital was frequented by visiting doctors from all parts of the United States, from England, France, Germany, and even as far away as Australia. In 1923 he published his monograph, "Practical Local Anaesthesia," which was recognized throughout the world as one of the best. For pioneer work his name was prominently mentioned as a candidate for the Nobel Prize. Although his name was most often associated with his numerous papers and addresses on local anesthesia, he was also recognized as an outstanding teacher in surgery. A goodly number of his publications covered the field of general surgery and surgical techniques.

In the advancement of local anesthesia he invented a high-pressure machine for the injection of solutions. Wire spring retractors for mechanical, nontraumatic exposure of viscera were his invention. These retractors are found in many surgeries and frequently used by those who are trained in their use. Other inventions of his are less well-known.

To accomplish his activities he frequently employed a professional artist, a master mechanic, researchers in medical and anatomical fields, stenographers, and assistants. The many thousands of dollars required to finance his endeavors were borne by him alone.

Dr. Farr was very active in the development of Minnesota Medicine, serving on its editing and publishing committee as long as his health permitted. Early in his career he developed an extremely painful condition in his spine. The pain, at times almost unbearable, caused him to stop midway in an operation before he could proceed. Often at any time or any place he would pound his hand against his back for pain relief. The first operation on the cord gave little relief. He died at St. Mary's Hospital shortly after his second operation.

Fate seemed to be very unkind to Dr. Farr. He operated on his sister and found an advanced malignancy. He financed the education of one of her sons in medicine who died during military service; he also financed the education in law of her second son who died in military service in England. His son, Paul, who was a medical student, drowned at Cedar Lake, and his wife died following an accident.

He helped finance the education of several medical students and aided several others to get started in practice. The profession lost an outstanding member, often misunderstood because he had the courage to stand up for what he thought was right. Those of us who knew him best marveled at his ability to accomplish so much in spite of so many adversities.

Dr. Farr was a member of the staff of St. Mary's and Asbury (now Methodist) hospitals but frequently operated on referred patients in other hospitals, both in and out of Minneapolis.

He was a member and past president of the Hennepin County Medical Society, a member of the Minnesota State Medical Association, the Minnesota Academy of Medicine, the Western Surgical Association, and the American Association of Obstetricians, Gynecologists and Abdominal Surgeons.

I am certain that a goodly number of doctors throughout the Northwest who were Dr. Farr's students or assistants feel as I do, that we appreciate and are grateful for the inspiration and training that we received through our association with him.

STANLEY R. MAXEINER, SR.

Transactions of the North Dakota State Medical Association

TRANSACTIONS OF THE NINETEENTH ANNUAL MEETING OF THE WOMAN'S AUXILIARY TO THE NORTH DAKOTA STATE MEDICAL ASSOCIATION

Grand Forks, North Dakota, May 2nd and 3rd, 1965

The first session of the Nineteenth Annual Meeting of the Woman's Auxiliary to the North Dakota State Medical Association was held in the new Grand Forks Country Club, Grand Forks, at 9:30 A.M., Monday, May 3, 1965, with Mrs. Clyde Smith, State President, presiding.

Doctor Dodds, outgoing State President of the North Dakota Medical Association, was on hand ready to present his address to our Auxiliary. He brought greetings from the Medical Association and stated in part of his travels how many of the medical ladies were trying to raise money for the Student Loan Fund. On one of his most recent experiences he talked of New Orleans, mentioning the medical ladies staging a chorus review for this purpose. The ladies have worked diligently in so many parts of our country. We must constantly make our auxiliary more interesting and challenging to hold members and to keep growing.

Dr. Harwood, Dean of the School of Medicine, University of North Dakota, reported on the Student Loan Fund and informed us that the need for students in North Dakota is greater than anywhere else in our country. Married students appear to get the most help from their families, plus the fact that most all of the wives are employed. Two-thirds of the average class have borrowed from the Student Loan Fund. Our medical students come from a lower economic level than any other on the national average. Dean Harwood went on to explain that a loan is revolving and that students do pay it back. He mentioned the insurance as $22.00 per year on $10,000 term insurance.

Roll was called with a quorum present. They were: State Officers: Mrs. Clyde Smith, President; Mrs. M. A. K. Lommen, President-Elect; Second Vice-President, Mrs. E. O. Hieb; Recording Secretary, Mrs. R. J. Ulmer.

Committee Chairmen: Mrs. M. A. K. Lommen, Membership; Nominating, Mrs. R. Hankins; Health Careers, Mrs. Sushen Thakor; Parliamentarian, Mrs. R. D. Schoregge; AMERF, Mrs. E. O. Hieb; By-Laws, Mrs. Carl London.

State and District Officers: Community Service, Mrs. Paul Ahlness; International Health Activities, Mrs. Calvin Fercho; Publicity, Mrs. John Lambie.

News, Views and Cues: Business and Circulation, Mrs. Jon Eylands.

Finance Committee: Mrs. C. Fercho, Chairman; Mrs. Paul J. Breslich.

District Presidents: Mrs. George Ivers, First District; Mrs. Donald McIntyre, Second District; Mrs. Charles Graham, Third District; Mrs. Carl B. London, Fourth District; Mrs. Paul Ahlness, Ninth District. Councilors: Mrs. C. Fercho, First District; Mrs. John Ruud, Third District; Mrs. Paul Breslich, Fourth District.

Mrs. Lee Christoferson gave the Student Loan Fund report. She made a motion to have each member pay $10.00 instead of $2.00. Mrs. Schoregge seconded this motion.

Mrs. Smith introduced Dr. Blair Henningsgard, As- He mentioned, in part, that Pennsylvania had combined toria, Oregon, who reported on AMPAC and COMPACT. this in their dues package and that they now have 75% membership. Cooke County is another illustration in that they have combined and grown. Doctors and their wives need to express themselves in governmental affairs as other groups of people do.

Our Auxiliary pledge was led by Mrs. Lommen.

The Auxiliary prayer was read by Mrs. E. Hieb.

A welcome to the meeting in Grand Forks was given by Mrs. R. Clark. Mrs. George Ivers of Fargo gave the response.

Mrs. Smith introduced her officers to the head table and the National guest, Mrs. Virgil Ray Forester, National Safety Chairman from Oklahoma City, Oklahoma.

Mrs. Sandmeyer gave the memoriam for Mrs. Mary Darrow Weible of Fargo (1881-1965). Flo Hankins sang the selection "Just A'Wearying For You" and was accompanied by Zoe Smith.

Iris Schoregge of Bismarck read the Convention Rules of Order.

Mary Lommen reported on membership.

Mrs. Thakor reported on Health Careers and stated that Jamestown had the Health Careers Convention held in the fall of 1964. The 1965 rally is to be held at Trinity Hospital in Minot. The students are very enthused and they do hope to keep growing each year.

Mrs. E. Hieb reported on the AMAERF. She made a recommendation that we give $5.00 per capita for AMAERF so it would help North Dakota. Mrs. Cleary moved to accept this recommendation and Mrs. Hankins seconded.

Mrs. R. J. Ulmer read the resolution directed from the House of Delegates to the North Dakota State Medical Association to Mrs. Clyde L. Smith and her successor.

RESOLUTION

WHEREAS, the ladies of the Woman's Auxiliary to the North Dakota State Medical Association, through devoted enthusiasm and continuous efforts over the years, have contributed diligently to the Medical Auxiliary Student Loan Fund of the Medical School of the University of North Dakota, and more recently to the American Medical Association Education and Research Fund, and

WHEREAS, these funds have enabled many medical students to complete their medical education, and

WHEREAS, the local Auxiliary Societies throughout the State have participated in many other commendable projects which reflect credit to their organization and to the medical profession,

NOW, THEREFORE BE IT RESOLVED that the House of Delegates of the North Dakota State Medical Association convey

to the Woman's Auxiliary our appreciation and thanks for their excellent work, and

BE IT FURTHER RESOLVED that a copy of this Resolution be directed to Mrs. Clyde L. Smith and her successor.

Mrs. London read the few changes in the By-Laws, which were adopted. Mrs. Hieb seconded the adoption of these items.

On Community Service, Mrs. P. Ahlness reported on the varied activities of our members.

In the absence of Mrs. H. J. Bertheau, Mrs. R. Schoregge of Bismarck reported on Rural Health.

Mrs. J. W. Cleary reported for Mrs. R. Tudor on the Legislative Report.

For International Health Activities, Mrs. C. Fercho mentioned that drugs and bandages seem to be the most practical things to send.

Mrs. J. A. Lambie reported as Publicity Chairman.

Disaster Chairman, Mrs. J. F. Schneider was absent. Mrs. C. Smith read her report.

The Safety Chairman, Mrs. A. C. Kohlmeyer, was absent. Mrs. G. Ivers read her report. It stated in brief that safety was not stressed this year on our district programs.

The SAMA report was read by Mrs. C. Graham in the absence of Mrs. T. H. Harwood.

Mrs. J. H. Mahoney was absent, but Mrs. C. Smith informed us that $237.35 was the total cost of handling the printing of *"News, Views, and Cues."* Blue Cross—Blue Shield paid the postage for us. The post convention issue will be handled by the present team.

Mrs. C. Fercho, Finance Chairman, gave her report. Mrs. M. Lommen moved to accept the budget report and Mrs. C. London seconded.

Mrs. M. Lommen read the Treasury Report in the absence of Mrs. R. Berg.

The meeting recessed for a luncheon which was held in the new Grand Forks Country Club.

Following the luncheon, the House of Delegates was called to order.

Mrs. Hankins presented the slate of officers. President, Mrs. M. A. K. Lommen; President-Elect, Mrs. E. Hieb; First Vice-President, Mrs. R. Clark; Second Vice-President, Mrs. L. Pray; Recording Secretary, Mrs. R. J. Ulmer; Treasurer, Mrs. R. Berg. Mrs. C. Smith made a motion to accept this slate of officers and Mrs. Ahlness seconded. The motion carried.

The First District Report was read by Mrs. George Ivers.

Second District report for Devils Lake was read by Mrs. C. Smith.

Third District report was given by Mrs. T. L. Schafer and mentioned that community service projects were stressed most of all this past year. Their district delegates were Mrs. G. G. Thorgrimson and Mrs. S. L. Pettit.

Fourth District report was given by Mrs. V. J. Fischer in the absence of Mrs. C. London.

Fifth District is still not organized.

Sixth District report was read by Mrs. J. W. Cleary for Mrs. S. J. Thakor. Their delegates were Mrs. J. W. Cleary and Mrs. W. D. Waldschmidt.

Seventh District Report was read by Mrs. E. Hieb in the absence of Mrs. R. D. Nierling. It stated in brief that they have twenty-one members and one Honorary Life member.

Eighth District had no report.

Ninth District report was read by Mrs. P. Ahlness. Their delegate was Mrs. R. E. Hankins of Mott. Mrs. Walter Hannewald was the alternate.

Tenth District: Mrs. K. Oja was absent.

There was no old business.

New business: Mrs. James R. Olson will be the Managing Editor of *News, Views, and Cues.* Mrs. John E. Ruud is District News Editor, and Mrs. John A. Lambie is Business and Circulation Manager. These members are residents of Grand Forks, North Dakota.

Mrs. Robert R. Ivers and Mrs. Perry O. Triggs of Fargo will comprise the Reading Committee.

Registration at the Woman's Auxiliary Medical Convention held in Grand Forks, May 2nd and 3rd was eighty-four members.

Mrs. C. Smith moved to adjourn the Board Meeting. Mrs. Paul Ahlness seconded the motion. The meeting adjourned.

MRS. R. ULMER, *Recording Secretary*

Convention Report

A delightful luncheon was served in the new Grand Forks Country Club at 12:30 P.M. with Mrs. Lommen, our President-Elect, presiding. She introduced officers and guests at the head table which included the guest speaker, President-Elect of the North Dakota State Medical Association, Dr. J. D. Craven, Mrs. Craven, and Mrs. Virgil Ray Forester, National Safety Chairman from Oklahoma City, Oklahoma.

The luncheon chairmen were introduced: Mrs. R. Painter and Mrs. B. Clayburgh. The convention chairman, Mrs. R. Clark, was also praised for her efficient work.

Dr. Craven brought greetings from the State Medical Association. He thanked the Auxiliary for the great amount of help to the Medical Loan Fund, the American Medical Association Education and Research Foundation, and the individual work in the field of public relations. This includes political legislation which the average doctor does not have the time to enter actively.

Mrs. M. A. Hohaug, wife of a Grand Forks orthodontist, vocalist, accompanied by Mrs. Kay Baukol, wife of a Grand Forks contractor, presented several delightful "spring" selections.

There were several ladies who won the lovely spring flower centerpiece arrangements.

The closing banquet was held in the East Grand Forks River Bend Country Club, East Grand Forks, Minnesota, at 6:30 P.M. Mrs. C. Graham introduced officer members and guests at the head table including Mrs. Virgil Ray Forester, National Safety Chairman.

Entertainment was outstanding by two local groups. A group of Candy Stripers from Crookston, Minnesota, in costume, danced and sang folk songs from various parts of our country. A "Funny Hat" skit was performed by some of the S.A.M.A. members.

Mrs. Forester stated, in part, how much she enjoyed visiting North Dakota and how much at home she felt. She tried to explain to our group that so much good can be done with so little effort on our part to prevent accidents in our homes and communities. Since many of our husbands treat the results of these casualties, we should attempt to consider safety programs in many of our local organizations—not just our Medical Auxiliary alone. Perhaps this is a future project that could save many lives as well as being helpful to others. This, too, could be another device in building better public relations.

The new State Officers were installed by Mrs. Forester. Mrs. C. Smith placed the President's pin on Mrs. M. Lommen. Mrs. Lommen thanked her for all her help and service the past year. Mrs. Lommen then presented Mrs. Smith with a Past-President's pin.

Gifts were given to Mrs. Forester and to Mrs. Smith as a small token of thanks.

It was announced that the Convention will be held next year in Fargo.

The Banquet Chairmen were Mrs. James Leigh and Mrs. E. A. Haunz. They are to be commended for another fine job.

Registration at the Woman's Auxiliary Medical Convention held here May 2nd and 3rd was eighty-four members.

We do want to again thank the Grand Forks ladies for a wonderful job so well done.

MRS. R. ULMER, *Recording Secretary*

Progress Report 1964-1965

Although the winter snows came early and lingered late in North Dakota, members of the Woman's Auxiliary to the North Dakota State Medical Association were not hibernating. Indeed a complete report of all their activities would fill volumes.

The groundwork was laid for our hoped-for team-membership at the Fall Board Meeting. At that time the Board voted in favor of having the state president present an official request to the House of Delegates of the North Dakota State Medical Association at their annual meeting in May asking them to adopt husband-wife memberships.

This request was made, and I am happy to be able to report the House of Delegates recommended without a single dissenting vote that all district members pay their wives' state and national dues. Hopefully, North Dakota will soon join the one hundred percent-ers.

Perhaps it was the memory of the golden grain waving in the North Dakota fields that inspired our members to such outstanding fund-raising efforts this year.

Under the guiding hand of our AMA-ERF Chairman, Mrs. E. O. Hieb, our donation to AMA-ERF was increased from $500 last year to $1,361 this year. The North Dakota Auxiliary also supports a loan fund for medical students at the University of North Dakota. Contributions to this fund amounted to $2,577, making a per capita contribution of $12.62 to both funds. Our North Dakota loan fund has a net worth over $30,000, but because this fund revolves, over $60,000 worth of loans have been made from it.

We should like to give special mention to the Sixth District Medical Society which acknowledged its gratitude to Sixth District Auxiliary members by presenting them with $200 for AMA-ERF in return for their services in providing woman-power at three mass tetanus clinics.

Of course, the most precious resources of the Woman's Auxiliary to the North Dakota State Medical Association are its individual members. We point with pride to our member Marilyn Swenson, of Jamestown, who was featured in the March Bulletin of the Woman's Auxiliary to the American Medical Association, as a typical, community-service minded auxiliary member. I hope you have all read the story of this beautiful, charming, and busy young mother who gives her time so unselfishly to those less fortunate.

The article is entitled appropriately, "The Rewarding Life of Marilyn Swenson." Multiply this rewarding life by the 316 North Dakota Auxiliary members and you will find 316 rewarding lives being lived in the boundaries of our state. The countless hours of volunteer service in churches, hospitals, schools, rest homes, fund drives, promoting safety, and distributing health education materials are given willingly with no thought of glory or material gain. But we receive our reward—it comes from the inner satisfaction of knowing we may have helped someone along our way.

We hope we have aided in the achievement of the goal of "Better Health, Better World" by extending the hand of friendship to the sick and suffering all over the world. At the request of our International Health Activities chairman, we brought sample drugs and bandages to the state convention. Twenty-six cartons were sacked and sent from there. An EKG machine is soon to be sent to World Medical Relief.

We hope we have encouraged many young people to follow medical paths through our Auxiliary sponsored Medical Career Clubs. There are six clubs in the state which provide lectures, tours of hospital facilities, demonstrations and films on many medical fields. We hope these youngsters will be inspired to use their talents to extend the work of our Auxiliary in far-flung places—so that in years to come we may truly say we helped make a better world through better health.

MRS. CLYDE L. SMITH, *President*

Financial Statement

MAY 1, 1964 — APRIL 30, 1965

Balance on Hand, May 1, 1964		$1,923.86
Dues:		
309 National	1,236.00	
12 Past Dues 1963-1964	28.00	
Cancelled Check	15.50	
Student Loan	20.00	
Playing Cards	30.45	
TOTAL		$3,273.81
Disbursements:		
Mrs. C. Smith, President		
National Convention	$ 250.00	
Expense Account 1964-1965	125.00	
Chicago Conference 1964	125.00	
Mrs. M. Lommen, President-Elect		
Chicago Conference 1964	125.00	
Purchase Bank Certificate		
Dakota Nat'l. Bank, Bismarck	1,000.00	
National Treasurer	321.00	
Miscellaneous Fund:		
Mrs. Jansonius (Telephone Bill)	9.50	
Bismarck Reminder (Letters)	5.01	
Mrs. Knudsen (Postcards)	2.50	
Mrs. S. J. Thakor (Letters, Postage)	15.50	
Atlantic Playing Card Co.	42.76	
Mrs. Halliday (Scrapbook)	4.00	
Mrs. McIntyre (Postage)	3.45	
Mrs. Hankins (Postage)	30.04	
News, Views and Cues	236.82	
A.M.A.E.R.F., Mrs. E. O. Hieb	25.00	
S.A.M.A., Mrs. T. H. Harwood	100.00	
Student Loan, Mrs. L. Christoferson	20.00	
TOTAL		$2,440.58
Balance on Hand, April 30, 1965		$ 835.23

Membership Report 1964-1965

On September 9, 1964 an Invitation to Membership in the Woman's Auxiliary to the North Dakota State Medical Association was mailed to the wife of each new licentiate in the State. There were thirty-eight.

On October 20, 1964 a list of all wives who were not members in the Districts was sent to each District Membership Chairman so that these prospective members could be contacted.

Eligibility for Auxiliary Membership is dependent upon

acceptance of an M.D.'s application in the District Society. In some cases the Society dues have been paid with the beginning of its fiscal year, January first. In this event the prospective Auxiliary member has been delayed in membership.

The Report of Membership is sent to National by the State Treasurer in March. The names of members paying dues after March first will not appear in the District Membership lists, JOURNAL-LANCET. It may not be understood that memberships can and need to be paid even after March first. The State dues of $3.00 (three dollars) comprise the monies upon which the State Finance Committee makes up the budget for the year. We have been barely breaking even.

From the Membership Report, submitted by the State Treasurer, the determination of the number of delegates (and alternates) to National Convention is made. There is one representative from each constituent auxiliary for each 300, or major fractions thereof. Each constituent auxiliary shall be entitled to at least one voting delegate in addition to its president. An alternate for each of these delegates is allowable.

Ours is a small state membership by comparison. Last year our State Auxiliary membership was 332; this year it is 316, a loss of 16 members. The membership in the North Dakota State Medical Association last year was 449; this year it is 455. We have a relative loss of 4.8% from last year, and a comparative 69.2% membership.

We have 9 organized Auxiliaries, and one unorganized. The District Membership totals are: First District—79; Second District—24; Third District—46; Fourth District—40; Fifth District—0; Sixth District—53; Seventh District—22 (one Honorary); Eighth District—18; Ninth District—23; and Tenth District—11. We have one National Honorary Member.

National has proposed a "team membership plan" which would bring the Auxiliary to 100% of the American Medical Association membership. This plan will close the gap in relative membership.

The "team membership plan" is that the M.D., when paying his dues at the county level, include the dues for his wife for State and National Auxiliary. The National dues are $2.00, one dollar of which includes subscription to the official organ—"The Bulletin"; and the North Dakota State dues of $3.00: a total of $5.00 per year.

Five states now have 100% in this team membership plan. They are: Montana, Idaho, Utah, Nevada and Arizona. You will note that each of these states is one of lower relative population. North Dakota is also of lower relative population.

From the *Report on Actions of the House of Delegates, American Medical Association, Eighteenth Clinical Convention, November 29—December 2, 1964, Miami Beach, Florida*—"Urged strong support of the Woman's Auxiliary and asked the state and county medical societies to give serious consideration to the idea of joint husband-wife membership."

In addition to showing an increased membership, a better State and National picture, this also presents a better basis for the planning of the Finance and Budgeting Committees, both at State and National levels.

National has indicated that this plan should begin at the local level.

On April 12, 1965 a letter presenting this information was sent to Dr. Ralph Vinje, President, Sixth District Medical Society. Sixth District Medical Society was asked to inaugurate this "team-membership plan." This "team-membership plan" will be presented by Mrs. Clyde Smith, Auxiliary President, to the House of Delegates, North Dakota State Medical Association in convention, Grand Forks, North Dakota on May 2, 1965. It is hoped that the House of Delegates will support this plan.

A complete list of every licentiate in the district was sent in April to each District Membership Chairman. The Auxiliary Membership was indicated. The chairman was requested to indicate which M.D.s were District Society Members, the marital status for purpose of Auxiliary prospective members, and to make any corrections in addresses. One copy was to be retained for District use and one returned to the State Membership Chairman.

MARY E. LOMMEN, *Chairman*

WASAMA Committee Report

In our April *News, Views and Cues,* our President, Mrs. Smith said, "The members of WASAMA are 'our grass-roots' and we shall cultivate them tenderly." After working with these young women, I feel future Medical Auxiliaries will be in capable hands. They are very enthusiastic, willing workers, full of sound ideas and blessed with high ideals!

Our group of about 35 had 16 meetings this past school year. The first Tuesday evening meeting is held at the Newman Center and on the third Tuesday evening of each month, is held at the home of a local physician. The members arrange their own programs and bring the refreshments and clean up the kitchen afterwards.

Those entertaining in their homes were the Mmes: Cornatzer, Campbell, Schafer, Evans, Vandergon, and Harwood. As an extra, we had a Christmas party at our home for the group. The group entertained our Medical Faculty Wives at a Fun Night in November and also co-sponsored with SAMA a farewell party for a Medical School faculty member. They had a dinner dance for all medical school students and faculty members in March. Their projects were—A Tasting Tea, Nov. 4, Christmas Cards were sold, and a rummage sale in April. $193.00 was grossed.

Our State Auxiliary contributed $100 to help defray expenses of two members to the annual WASAMA convention at Chicago this coming week. This generous check was deeply appreciated. A local insurance agent contributed $20 toward a printed news letter which comes out monthly, except January.

The members have given freely of their time to the Valley Day Care Center for Mentally Retarded Children.

Our group has received 3 appointments on regional and national levels. Regional Treasurer, Mrs. David Russell; National By-Laws Committee, Mrs. Richard Pearson; and Organization Editor of *Chatterbox,* Mrs. John Doerner.

These young women are a credit to our Auxiliary and deserve the continuation of our support. I thank each member who has helped the local WASAMA group.

Respectfully submitted,
MRS. T. H. HARWOOD,
Liaison—WMA

Woman's Auxiliary Program

SUNDAY, MAY 2, 1965

Headquarters — Ryan Hotel

12:00 NOON Registration, Lobby of the Ryan Hotel
Chairmen: Mrs. Harold Evans, Mrs. William Keig, Mrs. Louis Silverman, Mrs. James Olson

1:00 P.M. Nominating Committee, Gridiron Room, Ryan Hotel. Mrs. Hankins, chairman, Mrs. Van der Linde, Mrs. Poindexter, Mrs. Nierling, Mrs. Reichert

2:00 P.M. Finance Committee, Gridiron Room, Ryan Hotel
Mrs. Fercho, chairman, Mrs. Craven, Mrs. Hanewald, Mrs. Clark, Mrs. Berg, treasurer

3:00 P.M. Student Loan Fund Committee, Gridiron Room, Ryan Hotel
Mrs. Christoferson, chairman, Mrs. Goehl, Mrs. Poindexter, Mrs. Moses, Mrs. Breslich

4:00 P.M. Pre-Convention Board Meeting, Gridiron Room, Ryan Hotel

6:30 P.M. Informal Mixer and Buffet Supper. Upper level, Armory-Auditorium
For Doctors and their wives. Exhibitors and their wives. Guest Speakers and Invited Guests
Registration and Ticket Table will be set up here

MONDAY, MAY 3, 1965

8:15 A.M. Past Presidents' Breakfast, Dining Room of Ryan Hotel. Mrs. G. G. Thorgrimsen, chairman

9:00 A.M. Registration, Lobby of the Ryan Hotel, Grand Forks Country Club

9:30 A.M. Opening Session, Grand Forks Country Club
Student Loan Fund Discussion: Dean T. H. Harwood
Pledge of Loyalty: Mrs. M. A. K. Lommen
Invocation: Mrs. Oliver Uthus
Welcome: Mrs. Thomas Schafer, Incoming President of Third District Medical Auxiliary
Response: Mrs. George Ivers
Greetings: Dr. G. Alfred Dodds, President, North Dakota State Medical Association
In Memoriam: Mrs. John Sandmeyer
Roll Call
Reports

12:00 NOON Dutch Treat Cocktail Hour, Grand Forks Country Club

12:45 P.M. Luncheon, Grand Forks Country Club
Mrs. Robert Painter, Mrs. B. J. Clayburgh, chairmen
Mrs. M. A. K. Lommen, President-Elect, presiding
Address: Dr. Joseph Craven, President-Elect, North Dakota State Medical Association

2:30 P.M. Second Business Session, Grand Forks Country Club

6:15 P.M. East Grand Forks River Bend Country Club, East Grand Forks, Minnesota

6:30 P.M. Dutch Treat Cocktail Hour with Entertainment

7:15 P.M. Banquet, Mrs. Charles Graham, presiding
Address: Mrs. Virgil Ray Forester, National Safety Chairman and former National Auxiliary Liaison Officer to the National S.A.M.A. Auxiliary
Entertainment: "Funny Hat," Skit by S.A.M.A.
Chairmen of the Banquet: Mrs. James Leigh, Mrs. E. A. Haunz

There is going to be a Hospitality Room at the Ryan Hotel where members may meet to visit and relax over a cup of coffee and a cookie. This room will be available at 12:00 NOON, Sunday, May 2, and all day Monday, May 3.

Convention Committees

1. *Registration and Tickets*—Mrs. Harold Evans, Mrs. William Keig, Mrs. Louis Silverman, and Mrs. James Olson
2. *Hospitality and Courtesy*—Mrs. L. J. Prochaska
3. *Publicity*—Mrs. John Lambie
4. *Transportation*—Mrs. T. Q. Benson
5. *Finance*—Mrs. Kenneth Helenbolt
6. *Past Presidents' Breakfast*—Mrs. G. G. Thorgrimsen
7. *Luncheon*—Mrs. Robert Painter, Mrs. B. J. Clayburgh
8. *Banquet*—Mrs. James Leigh, Mrs. E. A. Haunz
9. *Convention Chairman*—Mrs. Rodney Clark

1964-1965 Officers and Chairmen of Standing Committees

STATE OFFICERS:

President: Mrs. Clyde Smith, 622 Raymond St., Bismarck
President-elect: Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck
First vice-president: Mrs. Oliver S. Uthus, 916 W. Central, Minot
Second vice-president: Mrs. Edwin O. Hieb, 211 Hillcrest Dr., Jamestown
Recording secretary: Mrs. Robert J. Ulmer, 714 S. 19th Ave., Fargo
Corresponding secretary: Mrs. J. M. Knudsen, 1143 E. Coulee Rd., Bismarck
Treasurer: Mrs. Roger M. Berg, 219 W. Ave. B, Bismarck

COMMITTEE CHAIRMEN:

Membership: Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck
Program: Mrs. Oliver S. Uthus, 916 W. Central, Minot
Nominating: Mrs. Robert Hankins, Mott
Parliamentarian: Mrs. R. D. Schoregge, 621 Ave. F West, Bismarck
Liaison to S.A.M.A.: Mrs. T. H. Harwood, 2704 Belmont Rd., Grand Forks
Historian: Mrs. D. J. Halliday, Box 217, Kenmare
A.M.A.-E.R.F.: Mrs. Edwin O. Hieb, 211 Hillcrest Dr. N.E., Jamestown
Health Careers: Mrs. Sushen J. Thakor, 907 Griffin St., Bismarck
By-laws: Mrs. Carl London, 506 S. Main St., Minot
Publicity: Mrs. John A. Lambie, 2721 Chestnut, Grand Forks
Rural Health: Mrs. Herman J. Bertheau, Linton
Legislation: Mrs. Robert Tudor, 714 W. Ave. C, Bismarck
Mental Health: Mrs. Robert DeLano, Northwood
Disaster preparedness: Mrs. Joseph F. Schneider, 1002 13th St. S., Moorhead, Minn.
International Health Activities: Mrs. Calvin Fercho, 1747 S. 7th St., Fargo
Safety: Mrs. A. C. Kohlmeyer, 1720 3rd St. S., Moorhead, Minn.
Official publication: *News, Views and Cues*
Managing editor: Mrs. James H. Mahoney, 601 8th St., Devils Lake
District news editor: Mrs. Jens Sahl, 210 Ninth St. N.W., Minot
Business and circulation: Mrs. Jon V. Eylands, 710 W. 3rd St., Rugby

DISTRICT PRESIDENTS, COUNCILORS AND CHAIRMEN OF SPECIAL COMMITTEES

First District: Mrs. George U. Ivers, 1106 S. 10th St., Fargo
Second District: Mrs. Donald G. McIntyre, 126 W. 11th St., Rugby
Third District: Mrs. Charles Graham, 923 Almonte Ave., Grand Forks
Fourth District: Mrs. Carl B. London, 506 S. Main St., Minot
Sixth District: Mrs. Ralph J. Dunnigan, 915 Ave. B West, Bismarck
Seventh District: Mrs. R. D. Nierling, 415 S.E. 9th, Jamestown
Eighth District: Mrs. A. K. Johnson, 1004 Fourth Ave. E., Williston
Ninth District: Mrs. Paul Ahlness, Bowman
Tenth District: Mrs. Karl F. Oja, Portland

DISTRICT COUNCILORS 1965-66

First District: Mrs. Calvin Fercho, 1747 S. 7th St., Fargo
Second District: Mrs. Connor Corbett, 316 Seventh St., Devils Lake
Third District: Mrs. John Ruud, 2221 Chestnut, Grand Forks
Fourth District: Mrs. Paul Breslich, 818 4th St. S.E., Minot
Sixth District: Mrs. R. F. Nuessle, 815 Griffin St., Bismarck
Seventh District: Mrs. G. H. Holt, 214 Second Ave. S.W., Jamestown
Eighth District: Mrs. Chester Borrud, 729 W. 16th St., Williston
Ninth District: Mrs. Walter Hanewald, R.R. 1, Box 18, Dickinson
Tenth District: Mrs. R. W. McLean, Hillsboro

SPECIAL COMMITTEES

Reading: Mrs. Joseph Cleary, 104 Seminole Ave., Bismarck; Mrs. R. F. Nuessle, 815 Griffin St., Bismarck; Mrs. William Buckingham, 901 Parkview, Bismarck; Mrs. Phillip O. Dahl, 1127 W. Highland Acres Rd., Bismarck

Resolutions: Chairmen to be appointed later by the Grand Forks convention committee

Nominations: Mrs. R. E. Hankins, Mott, chairman; Mrs. J. M. Van der Linde, 1016 4th Ave. N.E., Jamestown; Mrs. R. W. McLean, Hillsboro; Mrs. M. H. Poindexter, 1350 S. 9th St., Fargo; Mrs. R. D. Nierling, 415 9th St. S.E., Jamestown; and Mrs. L. H. Reichert, 543 W. First Ave., Dickinson. Alternates: Mrs. R. O. Goehl, 1015 Reeves Dr., Grand Forks; Mrs. J. A. Sandmeyer, 1005 Lanark, Grand Forks; and Mrs. J. D. Craven, 915 W. Second Ave., Williston

Finance: Mrs. C. K. Fercho, 1747 S. 7th St., Fargo, chairman; Mrs. Walter Hanewald, R.R. 1, Box 18, Dickinson; Mrs. Joseph D. Craven, 915 W. Second Ave., Williston; Mrs. Rodney G. Clark, 511 S. 18th Ave., Grand Forks; and Mrs. Roger Berg, 219 W. Ave. B, Bismarck

Student Loan: Mrs. Lee Christoferson, 1307 S. 6th St., Fargo, chairman; Mrs. R. O. Goehl, 1015 Reeves Dr., Grand Forks; Mrs. M. H. Poindexter, 1350 S. 9th St., Fargo; Mrs. James J. Moses, 1111 W. Highland Acres Rd., Bismarck; and Mrs. Paul J. Breslich, 818 4th St. S.E., Minot

Annual Report AMAERF 1964-65

This year of 1964-65 finds AMAERF in North Dakota with a substantial increase in their total contribution but not yet on a five dollar per capita basis which we had hoped to achieve.

Sixth District, Bismarck, was the only county auxiliary that supported a fund raising project, a rummage sale, which netted the major portion of their contribution. Seventh District had a Christmas cookie sale and, as in the remaining districts, members donated their contribution in return for note paper or memorials.

Total contribution from the State: $1,161.17. This is a per capita contribution of $3.78.

District	*Number of Members*	*Total Amount*	*Per Capita*
7th	21	$109.50	$5.21
6th	53	271.07	5.13
4th	40	202.00	5.05
2nd	25	121.60	4.86
1st	79	262.00	3.31
9th	21	60.00	2.85
10th	11	28.00	2.54
3rd	46	67.00	1.45
8th	13	15.00	1.15

Awards

1. Bismarck, Sixth District, Largest contribution.
2. Jamestown, Seventh District, Largest per capita contribution.
3. Bismarck, Sixth District, Greatest increase over last year.

Respectfully submitted,
Patricia M. Hieb
N.D. State AMAERF Chairman

Health Careers 1965

Again the time has come to summarize our year of labor. It is of utmost pleasure for me to do this, for I feel we have participated in an outstanding program in Health Careers.

There is an old adage that a thing worth doing should be done well. This applies equally well in the health field.

We began our 1964-1965 year by attending the 6th Annual Careers Rally in September at Jamestown. We had a registration of 125 enthusiastic boys and girls. It was held in the very stimulating surroundings of Jamestown College. The program this year was geared to nursing. However, they did have an opportunity to tour the State Hospital and inspect its facilities, especially its Occupational Therapy Department, in detail. Later in the day, they toured the Crippled Children's School and saw first hand how OT is taught to an eight-year-old girl. Everyone who was able to attend felt it was a profitable day. Plans are going forward for the 1965 rally to be held in Minot at the Trinity Hospital. I do hope you will feel that this is a worthy project and try to see that your districts are represented. It will prove to be one of the outstanding rallies, I am sure.

One of the very ambitious career groups in our state sold magazine subscriptions during the past year and earned enough money to attend the rally and also give their annual scholarship to an outstanding candidate. Other districts were active in securing educational programs, covering all phases of health careers and were instrumental in arranging tours of their local facilities.

Much material was given out and from the look at what the seniors in high schools are planning, I am sure this material has been put to good use. After reading summaries of the reports of the fifty states and what their activities in Health Careers have been, we can be very proud of our programs in the state.

The past year I have had many inquiries into our career programs and feel that what we are doing statewide is getting much recognition.

I have found it an extreme joy to work in the Health Careers field and hope our State continues to grow under the guiding hand of the Medical Auxiliary.

Sincerely,
Mrs. S. J. Thakor
Health Chairman

Community Service Committee Report

Our District Auxiliaries primarily carried on Community Service as their respective areas presented a need. This meant that the state did not actively participate in many projects as organized on the national level, but served with dedication many different service organizations individually, and also worked collectively on projects such as:

1. Parties for patients at State Mental Hospital
2. Activities of wives of medical students
3. Health Careers programs
4. Immunization clinics
5. Medical Self-Help programs
6. Aid to School for the Blind
7. Mental Health programs

On the small individual level we have had chairmen of the following: Heart Fund, Cancer Fund, Red Cross, Mental Health, Easter Seals and Community Chest. Participation has also been widespread in Girl Scouts, Boy Scouts, churches, P.T.A., Hospital Auxiliaries and organizations such as A.A.U.W., P.E.O., League of Women Voters, Federated Clubs and Rainbow.

With so many of our members spread so widely across the state, they have done a remarkable job of responding to requests for community service in a multitude of ways. They are true leaders in their many communities and a credit to the Woman's Auxiliary to the N.D. State Medical Association.

Respectfully submitted,
Mrs. Paul Ahlness
State Community Service Chairman

State Publicity Report 1964-1965

A questionnaire was sent in March to each of the Councilors in the various districts requesting information on the amount and type of publicity received in each district during the past year.

A copy of the questionnaire is attached.

The publicity received has been quite satisfactory in all districts.

Most districts had publicity chairmen for local coverage of their activities and the Councilors took care of items sent to the state publication.

Auxiliary members across the state are involved in many community projects which may or may not be directly connected with medical activities.

Information was sent to newspapers in the state regarding advance publicity of the State Convention as well as news of events during Convention.

Forms were presented at Convention so that district delegates and other representatives will receive publicity in their local newspapers.

An item concerning the National Convention with names of the North Dakota delegates will be released at a later date.

Doris Lambie, *State Chairman*

Rural Health Report 1964-1965

This year our work has been mainly with Immunization Clinics. Tetanus Clinics were held throughout the state as were clinics (combined) for Diphtheria, Whooping Cough and Tetanus. The Auxiliary members gave much of their time to this project.

Health Career nights were held jointly with P.T.A. and directly with schools. Members worked also with Cancer and Mental Health.

Questionnaires were sent to doctors, juvenile workers, law enforcement officers, county officials and school principals to check on the use of Mental Health facilities available to them in the State.

The movie "The First Ninety Days" on Mental Health was shown to the public sponsored by Homemakers Clubs.

Mrs. Herman Bertheau

State Mental Health Report

The broadcasting of a series of recordings called "Mirror to the Mind" was our special project this year. This is a series of half hour programs made especially for radio. Each is introduced by Dr. Edward Annis and moderated by Mr. Robert Goldman, Contributing Editor of the Saturday Evening Post. Seven radio stations in North Dakota received the records last year. Three of these stations reported that they had already played them. I did not receive a reply from the other four stations as to when they were used. The First district arranged for the series to be repeated by KNOX, and worked with Lutheran Welfare to publicize the broadcasts. District Nine was able to make arrangements for stations KDIX in Dickinson and KNDC in Hettinger to broadcast the series. Station KBOM, Bismarck, in the Sixth district, is also including the broadcasts in their schedule.

I am certain that many individual Auxiliary members do volunteer Mental Health work which is not reported. District Seven reported that they give a birthday party at the State Hospital, and also put on a program for Senior Citizens. District Nine has two members on the District Mental Health Planning Board which works with the State Public Health Board.

Mrs. Robert De Lano, *Chairman*

Legislative Report

Eldercare versus Medicare was the main interest of the Woman's Auxiliary to the North Dakota State Medical Association this past year. It was the reason for many planned "letterwriting," coffee parties and, as usual, the women responded willingly and enthusiastically. Pamphlets explaining why Eldercare offered better care than Medicare were distributed to members who, in turn, passed them on to friends and neighbors. In addition, an extensive article was published in the Auxiliary Newsletter explaining both bills. It was an effective way to reach every member of the Auxiliary. On some occasions the district legislative chairmen were called, and they, in turn, called their members to ask them and their friends to send telegrams to their senators and congressmen.

As of April sixteenth, Medicare Hearings have been delayed and no definite time has been set for public hearings on the Social Security Amendments of 1965.

In addition to working at the request of their legislative chairmen, numerous members were very active in their political parties working on the precinct and statewide levels. I believe that this is the most important and most effective way to promote the special interests which we, as doctors' wives, have. We shall always play an important part in shaping medical legislation. It is extremely important that all doctors' wives are informed on these matters and work to promote them. It is a worthwhile and rewarding interest.

Mrs. Robert Tudor
Legislative Chairman

International Health Activities 1964-1965

At report deadline I have heard from 5 of the 10 districts regarding International Health Activities. Three districts have appointed IHA chairmen and two work through other committees, such as Community Service.

The IHA needs and outlets were similar to last year. Drug samples and bandages seem to be the most practical for us to send from North Dakota. Last May, in Minot, we sent 19 boxes of drug samples to World Medical Relief, 11745 12 St., Detroit, Michigan, with the North Dakota Auxiliary paying the shipping costs. This year we hope to send as many drugs from Grand Forks. Many district reports told of plans to bring samples to convention again, and at least 6 boxes of supplies and drugs have been sent through the year by the districts. One district has sent drugs and bandages to a missionary in Ethiopia, known to their community, thru WMR.

Two areas of IHA which have not been emphasized this year are International Hospitality, and Project Hope of the People to People Health Foundation.

Our National Auxiliary President's motto this year was *"Better Health—Better World."*

Respectfully submitted,
Mrs. Calvin K. Fercho
North Dakota IHA Chairman

Safety Committee Report

The field of Safety, to say the least, was definitely not one of the interests of the Woman's Auxiliary to the North Dakota State Medical Association.

Last fall I sent to each district president a detailed list of Safety Program suggestions from the National Safety Chairman. Four of the 9 districts who replied to my recent inquiry had done nothing to include Safety in the year's program.

Late this year I received from the International Film Service a descriptive list of Safety films with special emphasis on Driver Education which may be either purchased or rented. Since all of us either drive, have children who do, or at least ride in automobiles, these films should be of interest. I would like to suggest when planning next year's program, each district consider the use of one of these excellent films.

If launching a Safety program per se seems like a large project, especially for the smaller districts, perhaps efforts could be combined with an already established civic Safety project such as Gun Safety, Traffic or Water Safety.

Mrs. Marian Kohlmeyer
State Safety Chairman

The Medical Auxiliary's Student Loan Fund Annual Report 1964-1965

The financial report for the Calendar year of 1964 is as follows:

A. F. Arnason, Assistant Dean, School of Medicine, University of North Dakota, reports that collections were good and we managed to pull out of the red, but the December 31 balance is now down to $376.24. He further states that our expenditures for all medical school activities now exceed our income and we are living on our surplus. When that is gone, we will have to get rid of one of our programs and the first to go will likely be the Medical Center loan fund or at least a part of it. Already, the Loan Board has discussed the possibility of limiting loans to students who agree to sign a pledge to return to practice in North Dakota. When that point is reached, and it is not far off, it would be nice to have more money in the Woman's Auxiliary loan fund. Most of the loans were for $500.

The contributions this year from each district were most commendable, and are as follows:

First District, Fargo	$ 790.00
Second District, Devils Lake	100.00
Third District, Grand Forks	405.00
Fourth District, Minot	400.00
Fifth District, Valley City	0
Sixth District, Bismarck	530.00
Seventh District, Jamestown	210.00
Eighth District, Williston	70.00
Ninth District, Dickinson	50.00
Tenth District, Hillsboro	22.00
TOTAL	$2,577.00

Mrs. Lee Christoferson
State Chairman

Medical Auxiliary Loan Fund Report

January 1, 1964 – December 31, 1964

NET WORTH:		
Notes receivable		$26,637.00
Cash		2,476.24
TOTAL		$29,113.24
EXPENDITURE REPORT:		
Cash Balance, January 1, 1964		(–$ 3,375.00)
Receipts:		
New Funds	$2,367.00	
Principal	6,619.39	
Interest	264.85	
TOTAL RECEIPTS		$ 9,251.24
		$ 5,876.24
Less Expenditures		3,400.00
CASH BALANCE, December 31, 1964		$ 2,476.24

Disaster Preparedness Report

In order to fill out the annual report of the Disaster Preparedness Chairman, I sent questionnaires to the District Presidents concerning the activities in their local group on disaster preparedness. We have not received any information from three districts. So far this year, none of us have taken active part in any civil defense programs.

Several months ago I received from National Headquarters a small pamphlet on Medical Self-Help training. The national goal is to train at least one member of each family in the United States in medical self-help. The course consists of 16 hours of instruction in the following subjects: shock, burns, infant and child care, bleeding and bandaging, transportation of the injured, fractures and splinting, artificial respiration, emergency childbirth, radioactive fallout and shelter, healthful living in emergencies.

Most of these courses have been taught in the High Schools, Colleges and through the Hospital Auxiliaries in our community. If in the smaller communities in North Dakota, you would like to make the Medical Self-Help Training a special project this next year, information on how to set up a program such as this and also special kits used, is available through the State Civil Defense office. It also states that the information and supplies are available without charge. If any of the district chairmen are interested, I would be happy to write to the State Civil Defense office and have them send literature to them.

In closing my report, I feel that even if we in our Woman's Medical groups aren't actively engaged in programming these courses, that in the event of disaster, regardless of type, we will all share in helping.

You in Grand Forks should be commended, young adults and parents alike, for hours of work spent in saving people and property in the recent flood disaster.

Sincerely,
Mrs. J. F. (Ann) Schneider
Chairman

By-Laws Report

Proposed and adopted By-Laws changes for the North Dakota Medical Auxiliary.

Article III—Section 4
change the one dollar to two dollars.

Article V—Section 2
change the four dollars to five dollars.

Article V—Section 4
change the one dollar to two dollars.

Article VII—Section 3—(9)—e.
change the one dollar to two dollars.

Article X—Section 1
The Standing Committees of this Auxiliary consist of the following:

(1) American Medical Association Education and Research Foundation
(2) By-Laws
(3) Disaster Preparedness
(4) Community Service
(5) Finance
(6) Legislation
(7) Membership
(8) Mental Health
(9) Nominating
(10) Health Careers
(11) Program
(12) Publicity
(13) Safety
(14) Medical Student Loan
(15) Rural Health
(16) International Health Activities

Article X—Section 2—(1)
change the name to American Medical Association Education and Research Foundation Committee—change the initials to A.M.A.-E.R.F.

Article X—Section 2—(3)
delete the present section

Article X—Section 2—(4)
change the name to Disaster Preparedness Committee.

Article X—Section 2—(11)
change the name to Health Careers.

Article X—Section 2—(15)
The Rural Health Committee shall work under the direction of the Council of Rural Health of the American Medical Association, to promote health education in the rural areas and to cooperate with approved groups whose aims are similar.

Article X—Section 2—(16)
The International Health Activities Committee shall evaluate activities of international philanthropic health projects and organizations, and inform constituent auxiliaries concerning activities in the field of international health needs.

With the deletion of the present (3) and with the new changes all the numbers in section 2 will change.

Mrs. Carl London
Chairman

Auxiliary President's Report—First District

First District Medical Auxiliary's 79 members have enjoyed four luncheon meetings. Our programs have been varied and most interesting.

Dr. Robert Ulmer was our first speaker.

Mrs. Lou Marget (Carole) gave us an entertaining lesson in drama.

We were pleased and honored to have our State President, Mrs. Clyde Smith, Mrs. R. D. Schoregge, and Mrs. E. O. Hieb at our January meeting. What Vikings, these three, who arrived by auto in blustery 30 degree below zero weather on schedule.

Dr. Hiram Drache, author of "Day of The Bonanza" delighted us with highlights from his book.

Mrs. Neill Goltz had a coffee party for the purpose of packaging bandage rolls for International Health Activities.

Mrs. O. A. Sedlak has been soliciting cakes for the Senior Citizens parties, sponsored by the Y.W.C.A. Our Auxiliary has provided these cakes for many years.

Mrs. B. A. Mazur, First District Mental Health, spearheaded the combined efforts of the First District Medical Auxiliary and the Mental Health Association for a radio program, a panel discussion pre-recorded. KXGO contributed one-half hour radio time each Sunday for thirteen weeks.

Mrs. F. A. DeCesare ordered and delivered Health Careers pamphlets to the local school counselors. They were happy to receive them.

We did not have a fund-raising project this year. We voted to assess the membership.

Our contribution to the Medical Auxiliary Loan Fund is $790.00 and to A.M.A.-E.R.F. $237.00.

We are so sorry to have lost our beloved member Mrs. R. E. Weible, who passed away March 4th. She will be sadly missed.

Officers for the coming year will be: Mrs. George Ivers, President; Mrs. L. G. Pray, Vice-President; Mrs. Donald Barnard, Secretary; Mrs. Frank Melton, Treasurer; Mrs. Calvin Fercho, Councilor.

Respectfully submitted,
Mrs. George Ivers, *President*

Auxiliary President's Report—Second District

The Devils Lake District Medical Auxiliary held four business meetings during the past year. The movie "The One Who Heals" was shown at our December meeting. Mrs. James Mahoney talked to us about her work on the Poverty Program with the Indians. It was very interesting for all of us. At our April meeting we were happy to have our state president, Mrs. Clyde Smith and Mrs. M. A. K. Lommen, president elect, as our guests.

A donation of $128.40 was made to AMA ERF compared to $15.00 last year. We also gave $101.00 to the Student Loan Fund.

Our district has 25 members; this includes 2 new members who joined this year. Devils Lake District lost 2 members through moves out of the state. Considering the fact that our district covers such a large area our attendance has been good. We're real proud of the fine job that Mrs. James Mahoney, Devils Lake, Editor of *News, Views and Cues* and Mrs. Jon Eylands, Rugby, as Circulation Manager have done the past year. Our members are also active in local community projects including Hospital Auxiliaries, P.T.A., Girl Scouts, Cub and Boy Scouts, Choral and Church Groups.

The new officers for 1965-66 are: Mrs. Ernest Gilbertson, Devils Lake, President; Mrs. David A. Rinn, Cando, Secretary-Treasurer; and Mrs. W. R. Fox, Rugby, Councilor.

Respectfully submitted,
Mrs. Donald G. McIntyre, *President*

Auxiliary President's Report—Third District

The Grand Forks Auxiliary to the District Medical Society has 46 members in good standing. This consists of nearly 100% membership within the city of Grand Forks.

We held four dinner meetings during the 1964-65 year.

Our first meeting was held October 15th at 7:00 P.M. at the Grand Forks Country Club. Mrs. Philip Woutat spoke on "Medicine in Politics." The second meeting was held on November 19th at 7:00 P.M. at the Golden Hour. Mr. Oscar Paulson, Project Engineer for the Missile Base, spoke on "Our Missile Program," showing a film in color on the construction of the Missile. Also Mrs. Eleanor Maves from Crookston, Minnesota brought her "Candy Stripers" over to put on a program of dancing and singing. They were very good and enjoyed by all. We donated $15.00 to their Scholarship Fund. On January 21st we expected a visit from our State President, Mrs. Clyde Smith, but due to illness in the family she couldn't be with us. A short skit was given at this meeting entitled "A Good Right Arm." The last meeting was held March 18th at the Westward Ho Motel. Annual reports were given and officers for the coming year elected. A program on Senior Citizens was given by Marge Ruud and her guest Mrs. Ruth Anderson, Nursing Consultant for Nursing Home Division of the North Dakota Health Department.

The Student Medical Wives have met several times in the doctors' homes which they enjoy very much. Two of their officers were with us for a dinner meeting. Our members donated rummage for their rummage sale April 10, 1965.

The auxiliary members have donated much of their time to Community Service, working in the fields of Hospital Auxiliaries, Heart, Cancer, Mothers March on Polio Drives, Church Auxiliaries, Y.W.C.A. and Y.M.C.A., Scout troops, Arena Booster project, etc.

The project committee decided this year to ask for a donation of $10.00 from each member for Student Loan Fund and dispense with the "Annual Dinner Dance." This was eliminated because of the work my Convention Committees are doing in preparation for the State

Medical Convention to be held in Grand Forks, May 1st, 2nd and 3rd. They received $405.00 in contributions for the Student Loan Fund.

Our Legislative Committee Chairmen, Mrs. E. L. Grinnell and Mrs. John Sandmeyer, have been very busy mailing out pamphlets on the Elder Care Bill which is supported by A.M.A. in opposition to Socialized Medicine. The women also voted to send $50.00 to the State A.M.A.-E.R.F. Fund.

The following women were elected to office for the year 1965-1966: President, Mrs. Thomas L. Schafer; Vice-President, Mrs. Richard K. Helm; Secretary, Mrs. George A. Wilson; Treasurer, Mrs. Kenneth S. Helenbolt; Councilor, Mrs. John H. Ruud.

I want to thank my officers and Committee chairmen for all the support they gave to me, thus making this year a very interesting and stimulating one.

Respectfully submitted,
MRS. CHARLES M. GRAHAM, *President*

Auxiliary President's Report—Fourth District

The Northwest District Medical Auxiliary has 40 paid members and 2 honorary members. As in previous years we have used the "package deal" to cover local, state and national dues, charging ten dollars.

We had four regular meetings this year and a combined meeting with the Medical Society.

Our first meeting was a luncheon, with the theme of "Getting To Know You," having many Air Force wives in attendance. Our legislation chairman, Mrs. Brian Briggs, gave an explanation of the Kerr-Mills Bill.

In December we held a joint meeting with the Medical Society and viewed a film on Medicare.

January saw us having an afternoon meeting and all present wrote letters to our Congressmen on our views of Medicare—Eldercare. We saw a film on the changing North Dakota picture.

In March we enjoyed a visit from our State President, Mrs. Zoe Smith. This meeting was held in the morning. A film about the Trinity Hospital Heart Center was shown and a tour followed.

Following the inspiration of our state president, a group of our members gathered together for a "ripping party" and made bandages.

At our April meeting we held our election and voted to contribute $50.00 to the summer camp for retarded and handicapped persons which is held in Minot. Our new officers are: President, Mrs. M. W. Garrison; Vice-President, Mrs. Roger Sorenson; Secretary, Mrs. Bernard Huss; Treasurer, Mrs. Brian Briggs; Councilor, Mrs. Samuel Shea.

We continue the policy of a $10.00 assessment for Student Loan. This is not compulsory and our total given this year was $400.00.

We contributed to A.M.A.-E.R.F. a total of $200.00.

We are co-sponsoring with the North Dakota Mental Health Association the series "Mirror of the Mind."

Respectfully submitted,
MRS. CARL LONDON, *President*

Auxiliary President's Report—Sixth District

Prior to our first meeting letters of invitation were sent to all prospective members and wives of residents.

A calling committee called each of these persons before each meeting.

During the year we had three dinner meetings and one luncheon.

Our first meeting was held on October 13, 1964. Our Health Careers Chairman, Mrs. Thakor, gave a report on her trip to Jamestown with her Health Careers Club members. Fifty-one members from Bismarck were present and our auxiliary gave $100.00 toward transportation.

Mrs. Saxvik, our Community Service Chairman, reported that D.P.T. and vaccinations were administered to school children on October 21-23, 1964; 1105 children attended. Seven members of our auxiliary assisted.

On December 9, 1964, we held our second dinner meeting. Mrs. Joseph Cleary, our I.H.A. Chairman, made an appeal for drug samples and bandages for medical relief. Her plea was heard, for at least six to ten women met twice a month to make bandages and hospital gowns from old sheets. These articles and drug samples will be sent to Dr. Warren Pierson and to Medical Relief.

Our third meeting was held on February 2, 1965, preceded by a social hour and dinner with our husbands.

Mrs. Wm. Waldschmidt reported progress was being made on the rummage sale for funds for our A.M.A.-E.R.F.

New officers for the coming year were elected at the April 2nd luncheon meeting. They are: Mrs. Sushen Thakor, President; Mrs. Charles Hamilton, Vice-President; Mrs. P. L. Owens, Secretary; Mrs. Wm. Waldschmidt, Treasurer.

Delegates to the state convention in Grand Forks are Mrs. Joseph Cleary and Mrs. Wm. Waldschmidt.

We held a rummage sale on March 19th and 20th. The enthusiasm of the girls was wonderful and we feel the total effort was worth it—netting $233.57 for A.M.A.-E.R.F.

The officers for the 1964-65 year were: Mrs. Ralph Dunnigan, President; Mrs. S. J. Thakor, Vice-President; Mrs. P. L. Owens, Secretary; Mrs. Wm. Waldschmidt, Treasurer.

There were five state board members from Sixth District. They are: Mrs. Clyde Smith, President; Mrs. M. A. K. Lommen, President Elect; Mrs. S. J. Thakor, Health Careers; Mrs. J. Knudsen, Corresponding Secretary; Mrs. Roger Berg, Treasurer.

Sixth District Auxiliary has fifty-three members and has contributed $530.00 to Student Loan.

Many thanks to the officers, special committee chairmen, the calling committee for *News, Views and Cues,* and the arrangements and reservations committee for all their efforts and good work.

Also, I would like to mention that Mrs. Thakor was chairman for the Cancer Drive; Mrs. Wm. Buckingham, chairman for the Heart Drive; and Mrs. Philip Dahl, Chairman for the Community Fund.

Respectfully submitted,
BERNADETTE DUNNIGAN, *President*

Auxiliary President's Report—Seventh District

The Seventh District feels very proud of our Jamestown Doctor's wife, Marilyn Swenson, who was chosen to represent all community-minded Medical Auxiliary members in the March issue of the Bulletin.

Our Medical Careers Club has grown in interest to High School students. An average of fifteen members attend meetings once a month, with two Auxiliary members as advisors. Marilyn Swenson reported 120 were in attendance at a very successful State meeting for Medical Careers' Clubs held at the State Hospital last September.

At Christmas we adopted two needy families and brought clothing, food and gifts to them.

In February, we and the Dental wives sponsored a Senior Citizens' party with 104 elderly people attending.

An enjoyable afternoon was spent including a program, games, and refreshments.

Our last project was a birthday party at the State Mental Hospital for about 120 patients with birthdays in April. We (and the Dental wives) brought cakes, ice cream and gifts. A program of music was presented by children of Auxiliary members.

The Seventh District has 21 members and one life member, Annabel Arzt. We have four meetings a year.

Officers for 1965-1966 are: President, Mrs. Philip Curtis; Vice-President, Mrs. Gerald Swafford; Secretary-Treasurer, Mrs. Robert Woodward; Councilor, Mrs. George Holt.

Respectfully submitted,
GRACE NIERLING, *President*

Auxiliary President's Report—Ninth District

The Ninth District with 21 members had only two meetings during the past year, due to inclement weather and the distances separating the members. The Auxiliary voted to drop active sponsorship of the Dickinson Future Nurses Club as it is now self supporting and quite active. However, individual members continue to work with various career groups in our area; we do not furnish financial support. Mental Health programs are being co-sponsored by the Auxiliary over two radio stations serving the area. Drug samples are being saved and shipped individually by several clinics. Health Education material has been distributed and it is hoped will soon be in evidence. The officers for the coming year are: President, Mrs. Hans Guloien; Vice-President, Mrs. Andrew Sawchuck; Secretary-Treasurer, Mrs. Larry Reichert; Councilor, Mrs. Walter Hanewald.

There were no obituaries in the Ninth District this year.

Respectfully submitted,
MRS. PAUL AHLNESS, *President*

Auxiliary President's Report—Tenth District

There are 9 members in the Tenth District Medical Auxiliary. Our group does not participate in the various activities but we have our regular meetings and we contribute to the A.M.A.-E.R.F. and Student Loan Fund. The slate of officers is the same at the present time.

Respectfully submitted,
MRS. KARL OJA, *President*

Post-Convention Board Meeting

Mrs. M. A. K. Lommen called the meeting to order.

The following were elected to the Nominating Committee: Mrs. Clyde L. Smith, Chairman, assisted by Mrs. V. J. Fischer. The members are: Mrs. Paul Ahlness, Mrs. Joseph D. Craven, and Mrs. D. G. McIntyre; alternates are: Mrs. H. Kermott, Mrs. Lester Wold, Mrs. F. DeCesare, and Mrs. M. Gieb.

Mrs. E. O. Hieb moved that we accept this slate of committee members and alternates. Mrs. Schoregge seconded. The motion carried. They were elected.

Mrs. Harold Evans will be the State Delegate to the AMA convention, medical auxiliary, in New York City, June 20 to 24, 1965. Mrs. M. A. K. Lommen will be the State Presidential Delegate. There is no alternate.

Mrs. P. Ahlness moved that the Post-Convention Board Meeting adjourn. Mrs. E. O. Hieb seconded the motion. The meeting was adjourned.

GRACE ULMER, *Recording Secretary*

1965-1966 Officers and Committee Chairmen

STATE OFFICERS:

President: Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck
President-elect: Mrs. Edwin O. Hieb, 211 Hillcrest Dr. N.E., Jamestown
First vice-president: Mrs. Rodney Clark, 1511 18th Ave. So., Grand Forks
Second vice-president: Mrs. Laurence G. Pray, 1701 S. 8th St., Fargo
Recording Secretary: Mrs. Robert Ulmer, 714 S. 19th Ave., Fargo
Treasurer: Mrs. Roger M. Berg, 219 W. Avenue B, Bismarck

COMMITTEE CHAIRMEN

Membership: Mrs. Edwin O. Hieb, 211 Hillcrest Dr. N.E., Jamestown
Program: Mrs. Rodney Clark, 1511 18th Ave. So., Grand Forks
Nominating: Mrs. Clyde L. Smith, 622 Raymond St., Bismarck
Parliamentarian: Mrs. Robert D. Schoregge, 621 Ave. F West, Bismarck
Liaison to S.A.M.A.: Mrs. T. H. Harwood, 2704 Belmont Rd., Grand Forks
Historian: Mrs. Harold Evans, 2624 Olson Drive, Grand Forks
A.M.A.E.R.F.: Mrs. George U. Ivers, 1106 S. 10th St., Fargo
Health Careers: Mrs. Paul Klosterman, 1529 No. 18th St., Bismarck
By-laws: Mrs. Paul Ahlness, Bowman
Mental Health: Mrs. S. J. Thakor, 907 Griffin Street, Bismarck
Legislation: Mrs. William P. Keig, 507 17th Ave. So., Grand Forks
Disaster Preparedness: Mrs. Ralph Mahowald, 606 S. 5th St., Grand Forks
International Health Activities: Mrs. Neill F. Goltz, 804 So. 8th St., Fargo
Safety: Mrs. Kenneth N. Amstutz, 412 8th Ave. S.E., Minot
Official Publication—*News, Views and Cues*
  Managing Editor: Mrs. James R. Olson, 1506 Chestnut St., Grand Forks
  District News Editor: Mrs. John E. Ruud, 2221 Chestnut, Grand Forks
  Business and Circulation: Mrs. John A. Lambie, 2721 Chestnut St., Grand Forks
Community Service: Mrs. R. O. Saxvik, 1243 W. Highland Acres Rd., Bismarck

SPECIAL COMMITTEES

Reading: Mrs. R. R. Ivers, 808 S. 8th St., Fargo; Mrs. Perry O. Triggs, 1402 S. 9th St., Fargo
Resolutions: Chairman to be appointed later by the Fargo convention committee
Nominations: Mrs. Clyde Smith, 622 Raymond St., Bismarck, Chairman; Mrs. V. J. Fischer, 303 8th Ave. S.E., Minot; Mrs. Paul Ahlness, Bowman; Mrs. Joseph D. Craven, 915 W. 2nd Ave., Williston; Mrs. Donald McIntyre, 126 W. 11th St., Rugby. Alternates are: Mrs. L. Henry Kermott, 200 7th Ave. S.E., Minot; Mrs. Lester E. Wold, 1708 So. 9th St., Fargo; Mrs. Frank A. DeCesare, 1401 S. 9th St., Fargo; Mrs. Marvin J. Gieb, 1219 S. 4th Ave., Fargo
Finance: Mrs. Walter Hanewald, 1043 5th Ave. W., Dickinson, Chairman; Mrs. Rodney G. Clark, 511 S. 18th Ave., Grand Forks; Mrs. Roger M. Berg, 219 W. Avenue B, Bismarck; Mrs. Thomas Pederson, 416 4th Ave. N.E., Jamestown
Student Loan: Mrs. M. H. Poindexter, 1350 S. 9th St., Fargo, Chairman; Mrs. James J. Moses, 1111 W. Highland Acres Rd., Bismarck; Mrs. Paul Breslich, 818 4th St. S.E., Minot; Mrs. Jon V. Eylands, 710 W. 3rd, Rugby; Mrs. Paul Ahlness, Bowman
Delegates to national convention, New York City, June 20-24, 1965: Mrs. Harold Evans, 2624 Olson Drive, Grand Forks, State Delegate; Mrs. M. A. K. Lommen, 831 Griffin St., Bismarck, Presidential Delegate. There were no alternates.

DISTRICT PRESIDENTS—1965-66

First District: Mrs. George U. Ivers, 1106 S. 10th St., Fargo
Second District: Mrs. E. V. Gilbertson, 845 4th St., Devils Lake
Third District: Mrs. Thomas L. Schafer, 1523 Cottonwood St., Grand Forks
Fourth District: Mrs. M. W. Garrison, 612 Mt. Curve Ave., Minot
Sixth District: Mrs. Sushen J. Thakor, 907 Griffin St., Bismarck
Seventh District: Mrs. Philip Curtis, 1005 9th Ave. N.E., Jamestown
Eighth District: Mrs. Rex Wiederanders, 901 1st Ave. E., Williston

Ninth District: Mrs. Hans Guloien, 41 5th Ave. W., Dickinson
Tenth District: Mrs. Karl Oja, Portland

DISTRICT COUNCILORS—1965-66

First District: Mrs. Calvin Fercho, 1747 S. 7th St., Fargo
Second District: Mrs. William R. Fox, 320 E. 9th St., Rugby
Third District: Mrs. John E. Ruud, 2221 Chestnut, Grand Forks
Fourth District: Mrs. Samuel Shea, 808 1st St. S.E., Minot
Sixth District: Mrs. Robert B. Tudor, 714 Avenue C West, Bismarck
Seventh District: Mrs. George Holt, 214 2nd Avenue S.W., Jamestown
Eighth District: Mrs. G. E. Ellis, N.E. of City, Williston
Ninth District: Mrs. Walter Hanewald, 1043 5th Ave. West, Dickinson
Tenth District: Mrs. R. W. McLean, Hillsboro

WOMAN'S AUXILIARY TO THE NORTH DAKOTA STATE MEDICAL ASSOCIATION 1965 MEMBERSHIP ROSTER

First District

Amidon, Mrs. Blaine F. ..... 1701 Ninth St. S., Fargo
Bacheller, Mrs. Stephen C. ..... Enderlin
Barnard, Mrs. Donald M. ..... 1212 S. 7th St., Fargo
Beithon, Mrs. Elmer J. ..... 429 N. 5th St., Wahpeton
Borland, Mrs. Verl G. ..... 1514 S. 9th St., Fargo
Bond, Mrs. John H. ..... 516 S. 13th St., Fargo
Burton, Mrs. P. H. ..... 415 S. 8th St., Fargo
Bushell, Mrs. Robert P. ..... 930 Park Drive, Fargo
Christoferson, Mrs. Lee A. ..... 1307 S. 6th St., Fargo
Christu, Mrs. Chris N. ..... 1509 S. 5th St., Fargo
Darrow, Mrs. Kent E. ..... 716 S. 8th St., Fargo
DeCesare, Mrs. Francis A. ..... 1401 S. 9th St., Fargo
Dodds, Mrs. G. Alfred ..... 1602 S. 10th St., Fargo
Ehlen, Mrs. Matt J. ..... 94 22nd Ave. N., Fargo
Fercho, Mrs. Calvin K. ..... 1747 S. 7th St., Fargo
Fjelde, Mrs. J. H. ..... 1526 S. 8th St., Fargo
Fortin, Mrs. H. J. ..... 1440 S. 8th St., Fargo
Gaebe, Mrs. Robert C. ..... 1702 S. 15th St., Moorhead, Minn.
Geib, Mrs. Marvin J. .. 1219 S. 4th Ave., Moorhead, Minn.
Geston, Mrs. Robert L. ..... West Fargo
Gillam, Mrs. John S. ..... 1433 S. 7th St., Fargo
Goff, Mrs. John R. ..... 1441 S. 8th St., Fargo
Goltz, Mrs. Neill F. ..... 804 S. 8th St., Fargo
Gustafson, Mrs. Maynard B. ..... Fargo
Hall, Mrs. G. Howard ..... 1748 S. 8th St., Fargo
Hamilton, Mrs. Thomas M. River Oaks, Moorhead, Minn.
Hawn, Mrs. Hugh W. ..... 1325 N. 1st St., Fargo
Heilman, Mrs. Charles O. ..... 49 N. 19th Ave., Fargo
Houghton, Mrs. James F. ..... 1707 S. 9th St., Fargo
Hunter, Mrs. Cornelius M. ..... 1434 S. 6th St., Fargo
Ivers, Mrs. George U. ..... 1106 S. 10th St., Fargo
Ivers, Mrs. Robert R. ..... 809 S. 8th St., Fargo
Jaehning, Mrs. David G. .... 823 N. 3rd St., Wahpeton
Kelly, Mrs. William C. ..... 313 Black Building, Fargo
Kohlmeyer, Mrs. Albert C. ..... 1720 S. 3rd St., Moorhead, Minn.
Lamb, Mrs. Donald L. ..... 1755 10th St. S., Fargo
Landa, Mrs. Marshall ..... 1720 S. 8th St., Fargo
Lane, Mrs. Mark H. ..... 521 Southwood Dr., Fargo
Lawrence, Mrs. Donald H. ..... 720 N. 7th St., Fargo
LeBien, Mrs. Wayne E. ..... 1353 N. 5th St., Fargo
LeMar, Mrs. John D. ..... 1324 N. 5th St., Fargo
Lewis, Mrs. T. H. ..... 1502 S. 6th St., Fargo
Lindsay, Mrs. Douglas T. ..... 1505 S. 11th St., Fargo
Long, Mrs. W. H. ..... 1438 S. 8th St., Fargo
Lytle, Mrs. Francis T. ..... 1306 N. 1st St., Fargo
Macaulay, Mrs. Warren L. ..... 1410 S. 9th St., Fargo
Magill, Jane, (Mrs. Gordon B.) .. 1312 S. 7th St., Fargo
Magness, Mrs. John L. ..... 1711 S. 6th St., Fargo
Mazur, Mrs. Bernard A. ..... 1237 N. 3rd St., Fargo
Melton, Mrs. Frank M. ..... 1702 S. 7th St., Fargo
Miller, Mrs. Joseph W. ..... 1436 S. 10th St., Fargo
Murray, Mrs. James B. ..... 1206 S. 15½ Ave., Fargo
Nagle, Mrs. Duane W. ..... 1101 N. 5th St., Fargo
Norum, Mrs. Henry A. ..... 801 South Drive, Fargo
O'Hearn, Mrs. Jerome O. ..... 89 29th Ave. N., Fargo
Oliver, Mrs. James ... 1817 3rd St. S., Moorhead, Minn.
Owens, Mrs. Walter L. ..... 2918 S. 12th St., Fargo
Poindexter, Mrs. M. H. ..... 1350 S. 9th St., Fargo
Pray, Mrs. L. G. ..... 1701 S. 8th St., Fargo
Rogers, Mrs. Robert G. ..... 1621 S. 7th St., Fargo
Schneider, Mrs. Joseph F. ..... 1002 S. 13th St., Moorhead, Minn.
Sedlak, Mrs. Oliver A. ..... 1019 S. 9th St., Fargo
Seifert, Mrs. Richard H. . 2024 S. 3rd, Moorhead, Minn.
Sessums, Mrs. John V., Jr. .... 810 19th Ave. S., Fargo
Shook, Mrs. Lester D. ..... 1326 S. 18th Ave., Fargo
Story, Mrs. Robert D. ..... 1312 S. 9th St., Fargo
Thompson, Mrs. George R. ..... 421 S. 14th St., Fargo
Thorfinnson, Mrs. Hugh D. ..... 1312 S. 7th St., Fargo
Traynor, Mrs. Mack V. ..... 1310 S. 9th St., Fargo
Triggs, Mrs. Perry O. ..... 1402 S. 9th St., Fargo
Ulmer, Mrs. Robert J. ..... 714 S. 19th Ave., Fargo
Webster, Mrs. William O. ..... 801 Park Dr., Fargo
Weible, Mrs. Ralph D. ..... 1628 S. 9th St., Fargo
Weible, Mrs. R. E. ... 1630 S. 9th St., Fargo (deceased)
Wenz, Mrs. E. P. ..... 1702 S. 13th St., Fargo
Wenzel, Mrs. Henry J. ..... 1414 S. 6th St., Fargo
Weyers, Mrs. Henry J. ..... 1414 S. 6th St., Fargo
Williams, Mrs. Neil S. ..... 1707 S. 13th St., Fargo
Wold, Mrs. Lester E. ..... 1708 S. 9th St., Fargo

Second District

Cook, Mrs. Stuart J. ..... Rolette
Corbett, Mrs. Conner A. ..... 316 7th St., Devils Lake
Eylands, Mrs. Jon V. ..... 710 W. 3rd St., Rugby
Fawcett, Mrs. John C. ..... 1125 5th St., Devils Lake
Fawcett, Mrs. Robert M. ..... 12th Ave., Devils Lake
Fox, Mrs. William R. ..... 320 E. 9th St., Rugby
Gilbertson, Mrs. Ernest V. .... 845 4th St., Devils Lake
Hillman, Mrs. R. S. Lyle ..... 204 2½ Ave. S.E., Rugby
Hilts, Mrs. George H. ..... Cando
Johnson, Mrs. Christian G. .... 819 W. 3rd St., Rugby
Kihle, Mrs. Kenneth W. ..... Bottineau
Klassen, Mrs. L. ..... 1012 3rd St., Devils Lake
Lazareck, Mrs. I. L. ..... 1032 5th St., Devils Lake
Longmire, Mrs. L. T. ..... 810 6th St., Devils Lake
McBane, Mrs. Robert D. .... 1106 4th St., Devils Lake
McIntyre, Mrs. Donald D. .... 126 W. 11th St., Rugby
Mahoney, Mrs. James H. ..... 601 8th St., Devils Lake
Neuenschwander, Mrs. Allen R. ..... Rolla
Palmer, Mrs. Dolson W. ..... Cando
Pine, Mrs. Louis F. ..... 817 7th St., Devils Lake
Rinn, Mrs. David A. ..... Cando
Sawchuk, Mrs. John ..... Rolette
Terlecki, Mrs. Jaroslaw ..... Minnewaukan
Turkula, Mrs. William .... 602 13th Ave., Devils Lake
Wolf, Mrs. Jerry D. ..... Bottineau

Third District

Benson, Mrs. T. Q. ..... 1524 Walnut, Grand Forks
Campbell, Mrs. Duncan W. ..... 1007 Chestnut St., Grand Forks
Clark, Mrs. Rodney G. .. 511 18th Ave. S., Grand Forks
Clayburgh, Mrs. B. J. .... 729 Reeves Dr., Grand Forks
Culmer, Mrs. A. E. Jr. .. 101 Reeves Court, Grand Forks

Dailey, Mrs. Walter C. . 1812 Belmont Rd., Grand Forks
DeLano, Mrs. Robert H. ..... Northwood
Doss, Mrs. R. Douglas .. 9 E. Conklin Ave., Grand Forks
Evans, Mrs. Harold .... 2624 Olson Drive, Grand Forks
Goehl, Mrs. R. O. ..... 1015 Reeves Dr., Grand Forks
Graham, Mrs. Charles M. 923 Almonte Ave.,Grand Forks
Graham, Mrs. John H. .. 1125 Reeves Dr., Grand Forks
Grinnell, Mrs. Ernest L. . 1207 Lincoln Dr., Grand Forks
Hamre, Mrs. Christopher J. ..... 811 Letnes Drive, Grand Forks
Harwood, Mrs. Theodore H. ..... 2704 Belmont Rd., Grand Forks
Haugen, Mrs. Clifford O. ..... Larimore
Haunz, Mrs. Edgar A. .. 1029 Lincoln Dr., Grand Forks
Helenbolt, Mrs. Kenneth S. 2509 Chestnut, Grand Forks
Helm, Mrs. Richard K. .. 1527 Chestnut Pl., Grand Forks
Keig, Mrs. William P. .. 507 17th Ave. S., Grand Forks
Lambie, Mrs. John A. .. 2721 Chestnut St., Grand Forks
Leigh, Mrs. James A. ..... 606 N. 3rd St., East Grand Forks, Minn.
Leigh, Mrs. Ralph E. ..... 301 Park Ave., Grand Forks
Liebeler, Mrs. Frances P. 1428½ S. 14th St., Grand Forks
Lorentson, Mrs. Carl E. . 1301 Chestnut St., Grand Forks
McLeod, Mrs. John J., Jr. . 217 27th Ave. S., Grand Forks
Mahowald, Mrs. Ralph E. .. 606 S. 5th St., Grand Forks
Meredith, Mrs. William C. ..... Drayton
Nelson, Mrs. Wallace W. 511 17th Ave. S., Grand Forks
Nelson, Mrs. William C. .. 1118 Reeves Dr., Grand Forks
Olson, Mrs. James R. .... 1506 Chestnut St., Grand Forks
Painter, Mrs. Robert C. . 1121 Belmont Rd., Grand Forks
Pettit, Mrs. Samuel L. .... 625 Reeves Dr., Grand Forks
Porter, Mrs. Charles B. .. 1210 Chestnut St., Grand Forks
Powers, Mrs. William T. ... 1509 Walnut, Grand Forks
Prochaska, Mrs. L. J. .... 620 Reeves Dr., Grand Forks
Ruud, Mrs. John E. ..... 2221 Chestnut, Grand Forks
Sandmeyer, Mrs. John A. ... 1005 Lanark, Grand Forks
Schafer, Mrs. Thomas 1523 Cottonwood St., Grand Forks
Silverman, Mrs. Louis B. 6236 Belmont Rd., Grand Forks
Tarpley, Mrs. Harold I. ... 511 Reeves Dr., Grand Forks
Thorgrimsen, Mrs. G. G. . 1615 4th Ave. N., Grand Forks
Vandergon, Mrs. Keith G. . 2220 Cherry St., Grand Forks
Wilson, Mrs. George A. .. 510 18th Ave. S., Grand Forks
Woutat, Mrs. Philip H. .. 1205 Lincoln Dr., Grand Forks
Youngs, Mrs. Nelson A. ..... 500 River St., Grand Forks

Fourth District

Amstutz, Mrs. Kenneth ..... 412 8th Ave. S.E., Minot
Barnes, Mrs. James A. ..... 9 Parkway, Minot
Boyum, Mrs. Lowell E. ..... Harvey
Breslich, Mrs. Paul J. ..... 818 4th St. S.E., Minot
Briggs, Mrs. Brian E. ..... 148 25th St. S.E., Minot
Cameron, Mrs. Angus L. .... 318 8th Ave. S.E., Minot
Cameron, Mrs. A. Malcolm .. 412 25th St. N.W., Minot
Dormont, Mrs. Richard E. ..... 202 9th St., S.E., Minot
Fischer, Mrs. V. J. ..... 303 8th Ave. S.E., Minot
Gammell, Mrs. Robert T. ..... Kenmare
Garrison, Mrs. M. W. ..... 612 Mt. Curve Ave., Minot
Giltner, Mrs. Lloyd ..... 9 Courtland Dr., Minot
Goodman, Mrs. Robert ..... Powers Lake
Gozum, Ekrem ..... 123 2nd Ave. S.E., Minot
Halliday, Mrs. Clara M. ..... Kenmare
Hart, Mrs. George M. ..... 213 7th Ave. S.E., Minot
Heidorn, Mrs. G. H. .... 1127 Valley View Dr., Minot
Hoopes, Mrs. Lorman L. .... 315 South Main St., Minot
Hordinsky, Mrs. Bohdan Z. ..... Drake
Huntley, Mrs. Wellington B. .. 208 7th Ave. S.E., Minot
Hurly, Mrs. William C. ..... 6 9th St. S.E., Minot
Jayapathy, Mrs. B. ..... 9 Souris Ct., Minot
Johnson, Mrs. O. W. ..... Rugby
Keck, Mrs. Stanley W. ..... 709 13th St. N.W., Minot
Kermott, Mrs. L. H. ..... 200 7th Ave. S.E., Minot
Kohl, Mrs. D. L. ..... 2200 4th Ave. N.W., Minot
Lampert, Mrs. Max T. ..... 101 10th St. N.W., Minot
Larson, Mrs. Richard S. ..... 500 W. 2nd, Velva
London, Mrs. Carl B. ..... 506 Main St. S., Minot
McCannel, Mrs. A. D. ..... 115 8th St. S.E., Minot
Olson, Mrs. Burton G. ..... 629 3rd St. S.E., Minot
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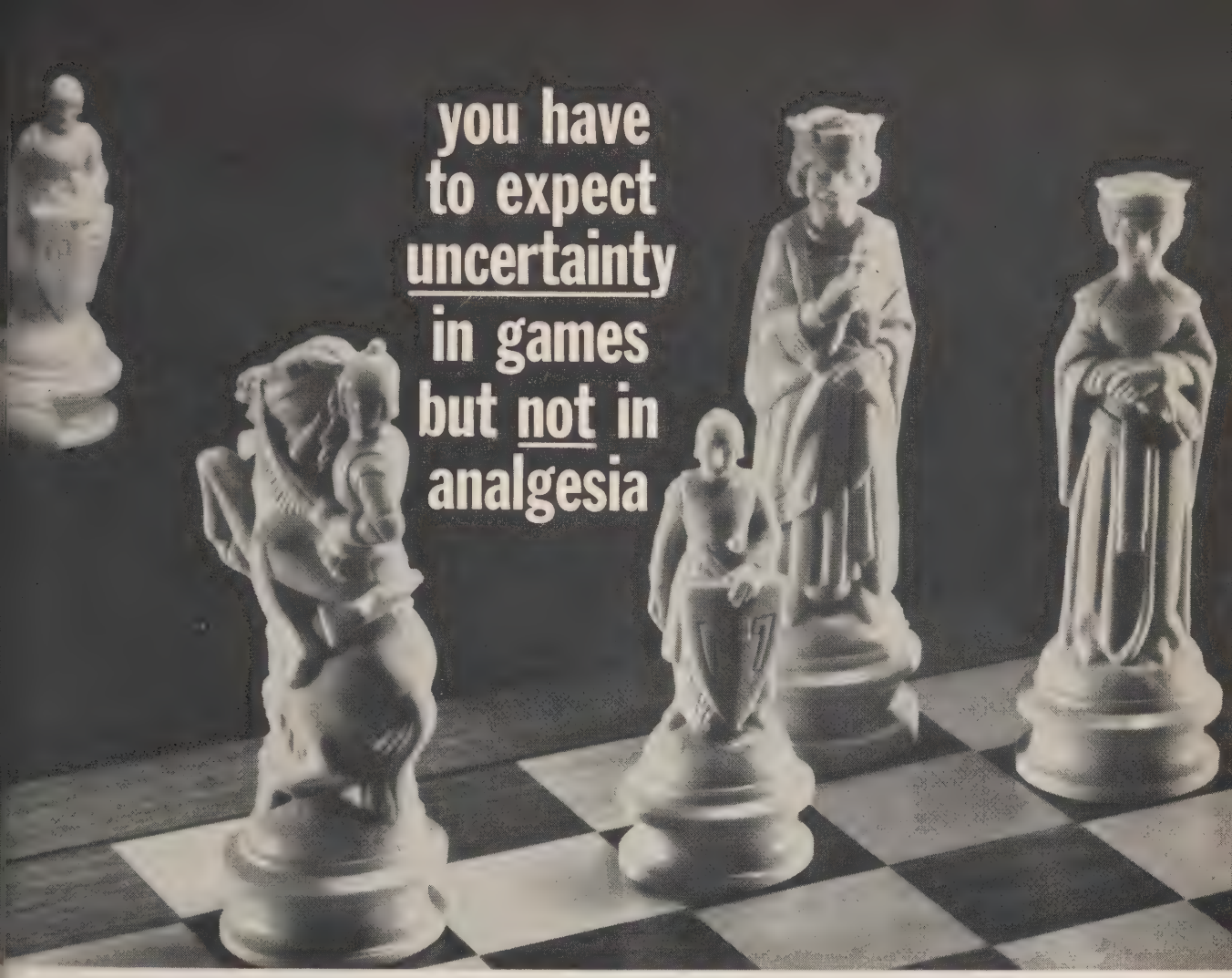
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Book Reviews . . .

Hematology in Practice

by STEVEN O. SCHWARTZ, WILSON H. HARTZ, JR., *and* JOSEPH H. ROBBINS, *329 pp., ill., McGraw-Hill Book Co., New York City, 1961. $14*

This book, approximately 300 pages long, is divided into 3 parts: first, the diagnostic approach, second, more detailed clinical entities, and third, a part on hemostasis. This is a very practical book, written for the clinician and medical student who are unfamiliar with the clinical approach to many of the hematologic problems.

The first part deals with differential diagnosis from the standpoint of a medical student or clinician as he examines the individual and evaluates the patient's condition from signs and symptoms obtained from the history and physical examination.

In the second section, a more concise description of the various hematologic diseases, along with their hematologic changes, is given in an attempt to permit a differential diagnosis that may be of value in treatment of the patient. One of the authors does an especially valuable job in making the illustrations. They are very simple and to the point in bringing out the various clinical findings that one should look for in hematologic diseases. The photographs and illustrations of many of the conditions are equally as good.

The last section on hemostasis clotting mechanisms is equally well done, as the authors have attempted to clarify many of the areas which have been overlapped, the usage of several terms meaning the same thing, and the laboratory tests that aid in diagnosis of various clotting defects.

This book is one of the clearest and most logical ones on hematology that has been written in the last several years. I feel that it can be recommended to all medical students, clinicians, and general men who are treating and seeing patients in their offices.

E. N. NELSON, M.D.
Minneapolis

The Prevention of Hospitalization

by MILTON GREENBLATT, M.D., ROBERT F. MOORE, M.D., ROBERT S. ALBERT, PH.D., *and* MAIDA H. SOLMON, B.A., *182 pp., ill., Grune & Stratton, New York City, 1963. $7.50*

The authors describe their well-known project, supported by a grant from the National Institutes of Health, consisting of the Community Extension Service which they instituted at the Massachusetts Mental Health Center. The project successfully demonstrated that the admission rate of a public mental health facility could be cut in half by a community psychiatry approach.

In his introduction, Dr. Greenblatt points out that the question of whether a patient should be admitted receives but a fraction of the attention normally given to the question of whether he should be discharged, despite the fact that the admission may be far the more crucial decision. "The strategic pivotal point is intake and towards this point there must be a whole new commitment of thought and energy." It is here that Dr. Green-

(Continued on page 18A)

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Dosage
Anturane, brand of sulfinpyrazone, is available as white, scored tablets of 100 mg. Initially, give half a tablet 4 times daily with meals or milk, increasing in one week to one tablet q.i.d. Increase to two tablets q.i.d. if necessary, and reduce if possible to as low as half a tablet q.i.d. after control. Continue through acute attacks, which can be concomitantly treated with phenylbutazone.

Patients on other uricosurics may be transferred to this drug at full dosage.

Contraindications
Active peptic ulcer. Salicylates and citrates antagonize the drug's action and are contraindicated for concomitant use.

Warning
Use with caution in pregnant women.

Precautions
Keep patients under close supervision and make periodic blood counts. Use cautiously in patients sensitive to pyrazoles, in patients with histories of peptic ulcer, and in conjunction with sulfa drugs, the sulfonylurea hypoglycemic agents, and insulin, the actions of which may be potentiated.

In mobilizing urate deposits, the drug may precipitate acute attacks of gout, urolithiasis, and renal colic, especially in the initial stages of therapy. Ensure adequate fluid intake and alkalinize the urine. With renal impairment, test renal function periodically.

Adverse Reactions
The most frequent are upper gastrointestinal disturbances. The drug may activate peptic ulcer. Rash occurs infrequently. Although not reported to date, blood dyscrasias are a possibility.

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in gout



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the most effective and best tolerated of the currently available uricosuric agents for the control of gout.‖*

Anturane, brand of sulfinpyrazone, was developed in the Geigy laboratories. Its pharmacologic activity is limited almost exclusively to increasing the urinary excretion of uric acid. For this reason, it is a drug of choice in chronic tophaceous gout and acute intermittent gout. It is not intended for relief of acute attacks of gout.

In most patients, the drug rapidly reduces serum uric acid levels to normal. This not only prevents new tophi but also mobilizes and promotes the excretion of urates already in the tissues. The reduction of tophi and periarticular crystals results in more mobile, less painful joints.

Anturane, brand of sulfinpyrazone, materially reduces the number and severity of acute attacks of gout. It may also be used to counteract hyperuricemia induced by certain diuretics.

Because of its potency, the drug is often effective in patients refractory to other uricosuric agents. Patients can usually be maintained indefinitely on it without cumulative effects or development of tolerance.

*Kuzell, W. C., et al.: Effect of sulfinpyrazone on serum uric acid in gout: a long-term study, Geriatrics 19:894, 1964.

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(Continued from page 16A)

blatt and his colleagues directed their thought and energy most effectively, and in a refreshingly new approach.

The program developed out of facilities primarily intended for former patients, for example the Half-way House and the Day Hospital. Such facilities were found to have value in preventing the full hospitalization of new patients. The goals for the program were: (A) to explore ways and means of preventing or circumventing hospitalization of acutely ill patients by (1) giving prompt psychiatric, social service, and nursing attention to patients recommended for admission, and (2) the judicious use of all available techniques and resources short of hospitalization and (B) to assess value of such techniques. The authors review their early decisions which established the guiding principles of the project and go on to report in detail on key aspects of it. The role of the various disciplines involved is analyzed, as well as several categories of patients. The part of the family and the referring physician in the prevention of hospitalization is examined and evaluated.

The book encompasses, in 176 pages, some background history of the Massachusetts Mental Health Center, its programs developed in the past twenty years, the inception of the idea of a community extension service, the planning and development of this service, and a very thorough assessment of its value—including a wealth of well tabulated statistical information. The subject matter is presented clearly and concisely, without literary flourish or unnecessary detail. The book should be read by psychiatrists, social workers, and others interested in the development of public mental health services.

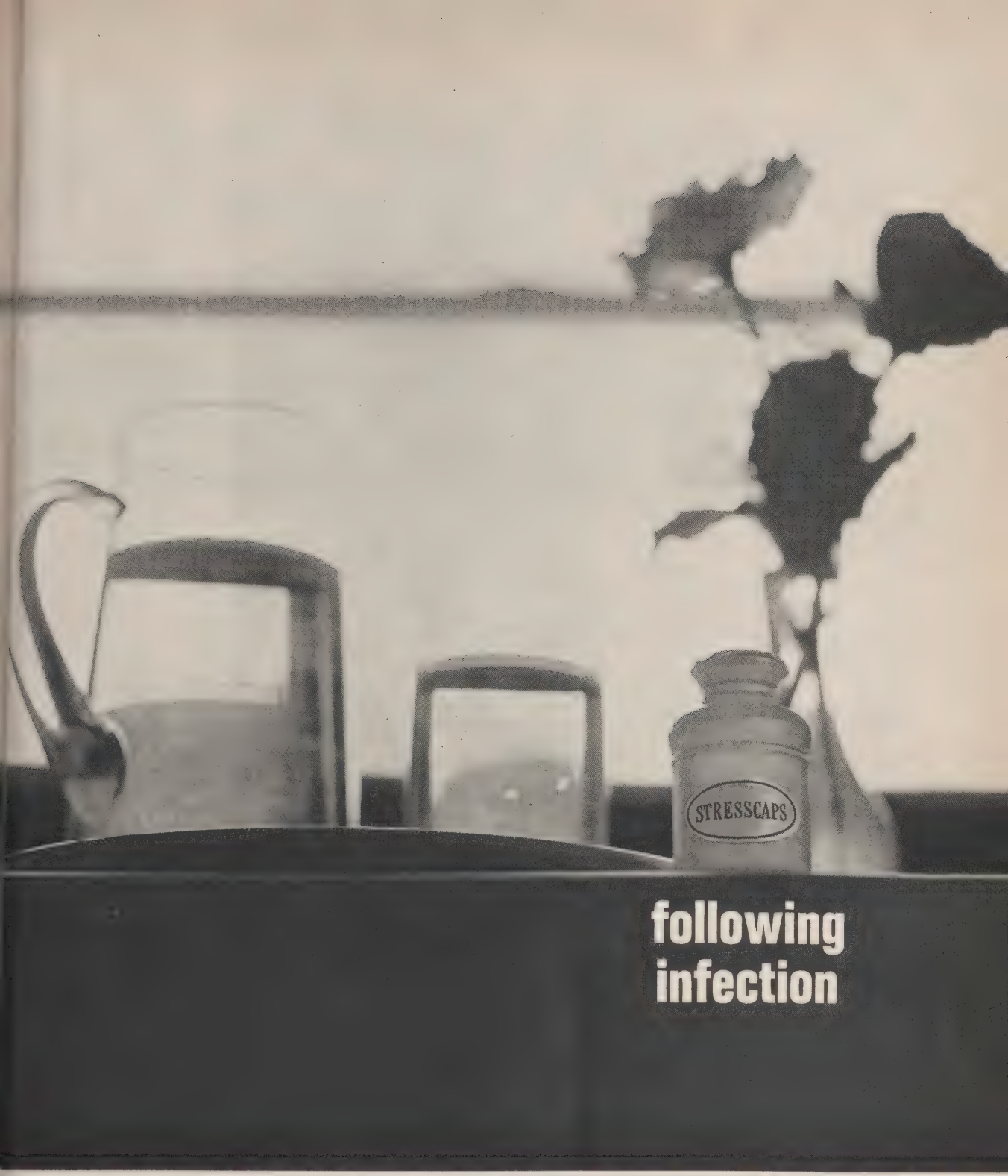
JOHN A. DOCHERTY, M.D.
Anoka, Minnesota

Ophthalmology: Principles and Concepts

by FRANK W. NEWELL, M.D., *491 pp., ill., C. V. Mosby Co., St. Louis, 1965. $12.25*

Dr. Newell has presented an excellent overview of the fundamentals involved in the practice of ophthalmology. The book was intended for students of medicine who will probably eventually devote their time to other fields, but I think it may have even greater value as a preview for the individual who thinks he may want to specialize in ophthalmology or has already decided to do so. The book is well written and easily understood. In most areas Dr. Newell goes into enough detail to explain the situation without assuming the role of the authority. Controversial points are handled nicely in that the reader is left with the impression that there really is some controversy and further study is needed to resolve it. All of the illustrations and especially the photographs are excellent. On several occasions, however, I found myself looking for more illustrations. For instance, there is an excellent illustration on how to begin the procedure of eversion of the upper lid. I think a second photo showing the lid everted and third one, perhaps, showing the lid double everted, would have added excellence to this portion of the text. Although the book was not intended to be a text on therapeutics, Dr. Newell does have a fine section on pharmacology. I think a little more detail on treatment of some of the more common office problems would have been beneficial.

ROBERT G. WOHLRABE, M.D.
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Niacinamide	100 mg.
Vitamin C (Ascorbic Acid)	300 mg.
Vitamin B_6 (Pyridoxine HCl)	2 mg.
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Recommended intake: Adults, 1 capsule daily, for the treatment of vitamin deficiencies. Supplied in decorative "reminder" jars of 30 (one month's supply) and 100 (three months' supply)

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"...it is extremely difficult and sometimes impossible to differentiate between 'pure depression' and anxiety and it is questionable whether depression without a certain degree of anxiety really exists."

Lehmann, H. E., Canad. Psychiat. Assn. J. *4(S)*: 1-12, 1959



An antidepressant designed for the clinical realities of office practice

As many physicians have reported, the large majority of neurotic depressed patients suffer from both depression and anxiety. It may be difficult to decide whether these patients are primarily depressed or primarily anxious. And yet drug treatment of only the symptom which seems more prominent may exacerbate the untreated element of the depression complex.

Consequently, it would seem that therapy specifically aimed at both the depression and associated anxiety and tension should increase success in treatment.

This is one of the important reasons why 'Deprol' has proved particularly helpful. For 'Deprol' acts rapidly both to lift the mood and to relieve the associated anxiety, tension and insomnia.

And side effects, at recommended dosage, have been infrequent and generally readily controlled.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

Supplied: Light-pink, scored tablets, each containing meprobamate 400 mg. and benactyzine hydrochloride 1 mg.

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News Briefs . . .

North Dakota

DR. CLEMENT B. HIGGIE has started practice at Michigan, N.D. Dr. Higgie, a native of London, England, had been in practice at Morse, Saskatchewan.

* * * *

DR. GERALD T. SAILER, former officer in charge of the U.S. Public Health Service Hospital at Belcourt, has joined the staff of the Hettinger Clinic at Dickinson. A native of Hazen, he graduated from Baylor University College of Medicine, Houston.

* * * *

DR. MARWIN A. K. LOMMEN, Bismarck, has been named president-elect of the North Dakota Society of Obstetrics and Gynecology. He will succeed Dr. Wallace W. Nelson, Grand Forks, next September.

* * * *

DR. ARMIN D. MEYER, former U.S. Air Force surgeon, has joined the Rodgers and Gumper Clinic at Dickinson as an associate. Dr. Meyer graduated from the University of Illinois College of Medicine.

* * * *

DR. ARNOLD M. THOMPSON, Bismarck, has begun private practice in Witt, Ill.

* * * *

DR. DEMOSTHENES HILIOPOULOS has started practice in Westhope. Dr. Hiliopoulos, previously associated with a hospital in Winnipeg, is a graduate of the Faculty of Medicine University of Thessaloniki, Greece.

* * * *

DR. PERCY L. OWENS, city health officer in Bismarck since 1940, has retired from full-time practice. Dr. Owens also was associated with the Missouri Valley Clinic. He is a member of the American College of Surgeons and the American Academy of General Practice.

* * * *

DR. WILLIAM E. G. LANCASTER, Fargo Clinic internist, has retired. Dr. Lancaster, 67, had been with the clinic for twenty-two years. He graduated from the University of Toronto Faculty of Medicine in 1922, and is a member of the American College of Physicians.

* * * *

DR. RONALD E. ILVEDSON, a graduate of the University of Texas Southwestern Medical School, Dallas, now is associated in practice with Dr. Charles Graham at Grand Forks.

* * * *

THREE PHYSICIANS HAVE JOINED the staff of the Dakota Clinic at Fargo. They are Drs. S. Fred Everett, Cleveland; Jack F. Glover, Jr., Dallas; and Charles A. Stevens, Jr., Minot. Drs. Everett and Glover specialize in internal medicine, and Dr. Stevens in obstetrics and gynecology.

* * * *

MEETINGS, 1965-66

December, 1965

11 Interim Council Meeting (North Dakota State Medical Association), Fargo

January, 1966

7-8 State Board of Medical Examiners, Grand Forks

NEWS BRIEFS

15 North Dakota Physicians Service Board of Directors (tentative)

Minnesota

DR. ROBERT R. KIERLAND, head of the section of dermatology of the Mayo Clinic, and professor of dermatology and syphilology in the Mayo Graduate School of Medicine, has been elected an honorary foreign member of the Polish Association of Dermatology and an honorary member of the Portugese Society of Dermatology and Venereology.

* * * *

DR. RAYMOND C. MAGNUSON, physician and surgeon at the Cambridge Clinic, left August 18 for a three-month mission in a leprosarium and clinic at Gendeberet, Ethiopia. The institutions are operated by the Baptist General Conference.

* * * *

DR. ALVIN L. SCHULTZ has been appointed director of the department of medicine at Hennepin County General Hospital, Minneapolis. He succeeds the late Dr. Frederick W. Hoffbauer. Dr. Schultz has been chief of medical research and education at Mount Sinai Hospital in Minneapolis since 1959.

* * * *

DR. JOSEPH A. STENZEL has become an associate at Meany and Meekin Medical Center in Columbia Heights. A former St. Louis Park high school teacher, he received his degree from the University of Minnesota Medical School in 1963.

* * * *

DR. ROBERT G. CARLSON of the Lakeland Clinic, Willmar, has started a two-year residency under Dr. C. Walton Lillehei at the University of Minnesota Medical School. Dr. Carlson is a fellow in the American College of Surgeons. He has been associated with the Lakeland Clinic since 1962.

* * * *

DR. QUENTIN F. KNAUER, Cleveland, is associated with Drs. Jose and Alayne Aruguete at Sandstone Clinic. Dr. Knauer graduated from Western Reserve University School of Medicine in 1958.

* * * *

DR. RANDOLPH M. MC CLOY has been elected president of the Association of Fellows of the Mayo Graduate School of Medicine, Rochester. Dr. McCloy is a fellow in gastroenterology.

* * * *

DR. LOUIS A. BRUNSTING, senior consultant in dermatology at the Mayo Clinic, Rochester, and professor of dermatology and syphilology in the Mayo Graduate School of Medicine, gave the fifth Paul A. O'Leary Memorial Lecture at the annual meeting of the Minnesota Dermatological Society.

* * * *

DR. JOHN S. LUNDY, founder and former head of the anesthesiology section at the Mayo Clinic, has been appointed clinical professor of anesthesiology at the University of Washington School of Medicine, Seattle.

* * * *

DR. EDWARD S. JUDD has received a Distinguished Alumnus Award from Geisinger Medical Center at Danville, Pa. Dr. Judd, professor of surgery at the Mayo Graduate School of Medicine, was an intern at George F. Geisinger Memorial Hospital in Danville from July 1936 to July 1937.

(Continued on page 25A)

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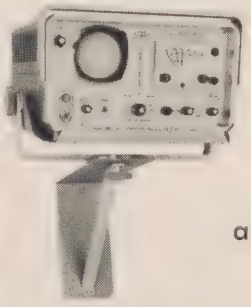
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NEWS BRIEFS

(Continued from page 23A)

A SYMPOSIUM on "The Adrenergic Blocking Agents with Special Reference to Hypertension and the Catecholamines" will be held at the Sheraton-Ritz Hotel, Minneapolis, Saturday, Dec. 4. The session is cosponsored by the American College of Cardiology and the Minnesota Heart Association. On the program are Drs. R. P. Ahlquist, University of Georgia School of Medicine; Karl Engleman, National Institutes of Health; Jesse Edwards, St. Paul; Naip Tuna, Minneapolis; and Sheldon Sheps and Richard Zimon, Mayo Clinic. Further information is available from the Minnesota Heart Association, St. Paul.

* * * *

DR. J. BRADLEY AUST, professor of surgery at the University of Minnesota Medical School, has been appointed chairman of the department of surgery at the University of Texas Southwestern Medical School, Dallas. Dr. Aust, a native of Buffalo, N.Y., received his degree from the State University of New York School of Medicine at Buffalo.

* * * *

DR. GEORGE W. STAHL, Austin, succeeded a Minneapolis physician, Dr. Bernard J. Spencer, as president of the Southern Minnesota Medical Association in September. Dr. Stahl, a urologist, is a graduate of the University of Wisconsin Medical School.

* * * *

DR. ROBERT H. NELSON, a Benson general practitioner, has accepted a one-year appointment as a physician for the Federal Aviation Agency at Wake Island.

* * * *

DR. FRANK R. KOTCHEVAR of the East Range Clinic, Eveleth, announced his retirement in August. A native of Ely, Dr. Kotchevar graduated from the Northwestern University Medical School, Chicago, and began his practice at Eveleth in 1928. He was elected a fellow in the American College of Surgeons in 1944.

* * * *

SAFETY MEASURES for lift-off and reentry in the Gemini space program were developed from studies conducted by Dr. Earl H. Wood, aeropsace medical researcher at the Mayo Clinic, and Dr. George L. Allen of Brooke Army General Hospital, San Antonio. Dr. Wood is on leave for additional study at the Physiology Institute at the University of Berne, Switzerland.

* * * *

DR. A. B. BAKER, chairman of the University of Minnesota Medical School division of neurology, is heading a university study of cerebral-vascular disease under a $298,172 research grant from the U.S. Public Health Service.

* * * *

DR. RONALD J. OHMANN has joined the Glencoe Clinic staff. A 1962 graduate of the University of Minnesota Medical School, he recently completed two years of Army service.

* * * *

DR. ROBERT R. RYNEARSON, assistant medical director at Rochester State Hospital, has accepted a staff position at Scott and White Memorial Hospital, Temple, Texas. Dr. Rynearson had been at Rochester State Hospital since 1962 when he completed his residency in psychiatry at the Mayo Graduate School of Medicine.

(Continued on page 26A)



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WANTED—1 or 2 general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D. Greenbush, Minn.

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(Continued from page 25A)

South Dakota

DR. JOHN J. SMITH has joined the Homestake Hospital staff at Lead. Dr. Smith, a graduate of the Tulane University School of Medicine, had been in general practice at Paris, Ark. Earlier, he was associated with the Veterans Administration Hospital at Little Rock.

* * * *

DR. JOUN T. MURPHY of the Veterans Administration Hospital, Columbia, S.C., has been appointed radiologist for both Methodist and St. Joseph's Hospitals at Mitchell. Dr. Murphy, a graduate of the Marquette University School of Medicine, is a member of the American Board of radiology.

Deaths . . .

DR. DANIEL E. GREENE, 50, Warren, Minn., died Aug. 31 at his home. Dr. Greene had practiced at Warren the last four years. He was a 1943 graduate of the University of Nebraska College of Medicine.

* * * *

DR. MELVYN E. WITTHAUS, 38, general practitioner at White Bear Lake, Minn., drowned Aug. 29 when his sailboat capsized on White Bear Lake. He was a graduate of the University of Minnesota Medical School, and had been in practice since 1953.

* * * *

DR. ROBERT R. REMSBERG, city health officer at Tracy, Minn., died of a heart attack Aug. 30 at his office. He was 52. Dr. Remsberg, a graduate of the University of Kansas School of Medicine, had been in general practice in Tracy since 1946.

* * * *

DR. JOHN A. MALMSTROM, 62, Virginia, Minn., died Aug. 21. He had established the East Range Clinic at Virginia. Dr. Malmstrom was born at Chisholm and had been in general practice at Virginia for thirty-eight years. He received his degree from the University of Minnesota Medical School in 1928.

* * * *

DR. ARCHIBALD W. GRAHAM, 86, Chisholm, died Aug. 25. Dr. Graham, a 1905 graduate of the University of Maryland School of Medicine, specialized in ophthalmology and was the school physician at Chisholm for fifty years. He was a native of Fayetteville, N.C.

* * * *

DR. FELIX F. VONNEGUT, 70, died Aug. 17 in Bismarck, N.D. A native of New Jersey, he had practiced at Hague and Linton since 1922. He was graduated from Medizinische Fakultat der Universitat Rostock in Rostock, Germany.

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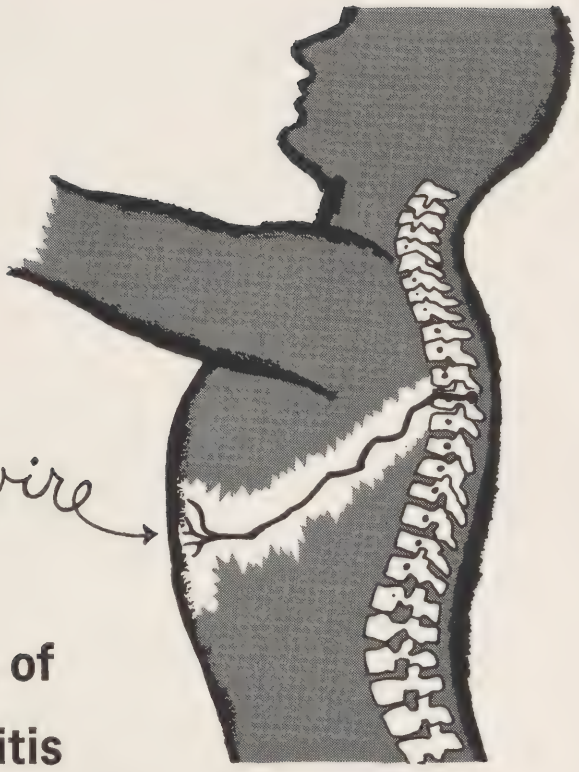
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Repeatedly in published clinical studies,[1-10] investigators stress the following therapeutic characteristics:

- relief of inflammatory pain (non-traumatic) is prompt—particularly when administered early.[1-4]
- disability time is shortened from weeks to days.[7]
- so specifically effective is Protamide that a positive response is diagnostic of inflammatory neuritis.[3,4]
- prompt relief is observed even in ophthalmic herpes zoster.[5,6]
- incidence of sequelae such as postherpetic neuralgia is reduced.[1-4]
- consistently described as the therapy of choice.[1,3-6]

Administration:

In neuritis and herpes zoster, one ampul I.M. daily for 2 to 5 days usually relieves pain completely in patients treated early. Well tolerated.[1-10] However, inadvertent intravenous administration may cause anaphylactoid reaction.

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References: (1) Baker, A. G.: Penn. Med. J. *63*:697-698 (May) 1960. (2) Smith, R. T.: New York Med. *8*:16-19 (Aug. 20) 1952. (3) Smith, R. T.: Med. Clin. N. America (March) 1957. (4) Lehrer, H. W.; Lehrer, H. G., and Lehrer, D. R.: Northw. Med. *54*:1249-1252 (Nov.) 1955. (5) Sforzolini, G. S.: Arch Ophthal. *62*-381-385 (Sept.) 1959. (6) Shupala, E.: W. Virginia Med. J. *56*:191-193 (June) 1960. (7) Xander, G. W.: Western Med. *1*:14-17 (Sept.) 1960. (8) Combs, F. C., and Canizares, O.: New York J. Med. (Mar. 15) 1952, pp. 706-708. (9) Marsh, W. C.: U.S. Armed Forces Med. J. *1*:1045 (Sept.) 1950. (10) Love, T. R.: Rocky Mountain Med. J. *50*:873 (Nov.) 1953.

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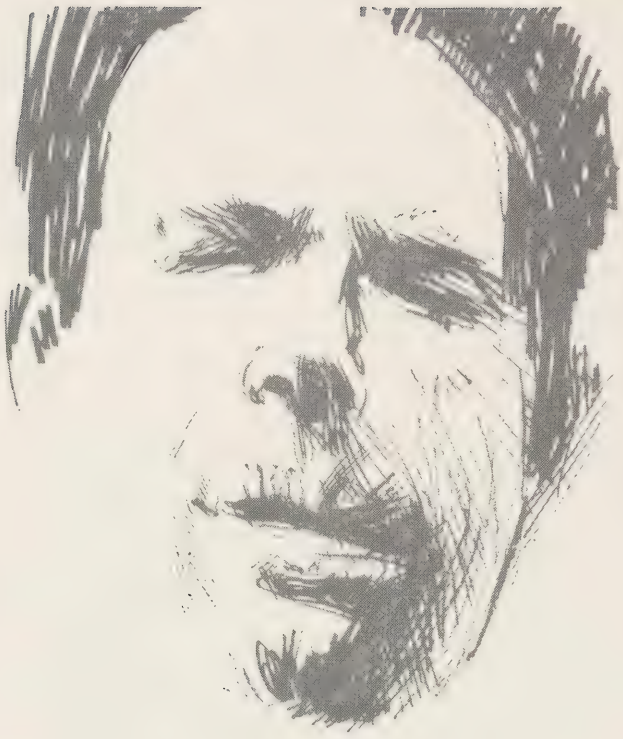
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INDEX MEDICUS



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Papaverine hydrochloride	16 mg.
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Vitamin C	100 mg.

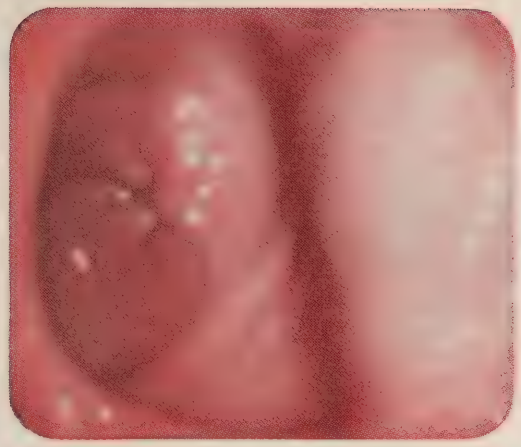
Dosage: Adults, 1 capsule 3 or 4 times daily; children, according to age and weight.

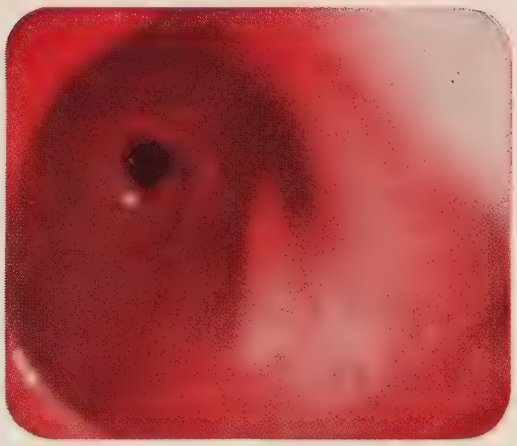
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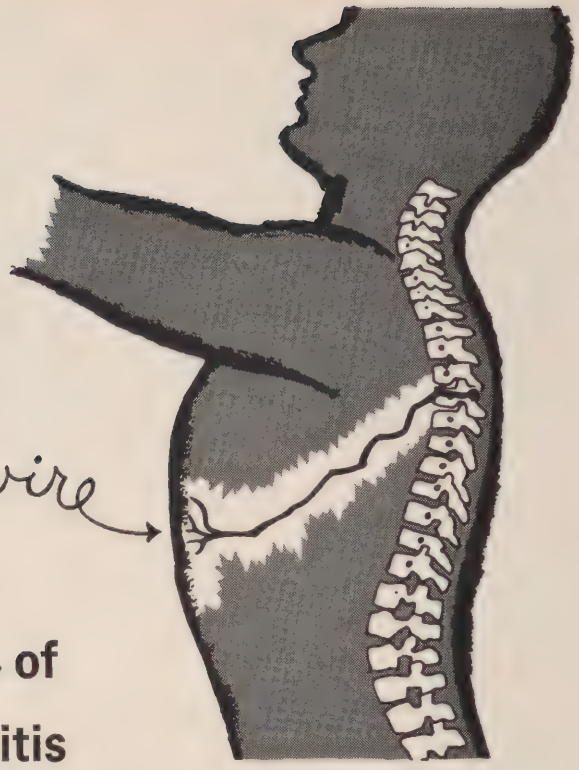
1. Barowsky, H.; Greene, L., and Bennett, R.: Investigators' Clinical Report. Photographs courtesy of Drs. H. Barowsky, L. Greene and R. Bennett.

2. Barowsky, H.; Greene, L., and Paulo, D.: Paper read at Meeting of American Society for Gastrointestinal Endoscopy, Montreal, Canada, May 25-27, 1965.

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Henry Swan, M.D.

Renal Insufficiency and Pancytopenia in Subacute Bacterial Endocarditis ... 579
Saul I. Nitzberg, M.D., and Paul L. Rodensky, M.D.

Primary Pulmonary Emphysema in Adolescence 583
Håkan Poppius, M.D., and Antero Muittari, M.D.

The Changing Scene in Medicine 1887-1960 586
S. Marx White, M.D.

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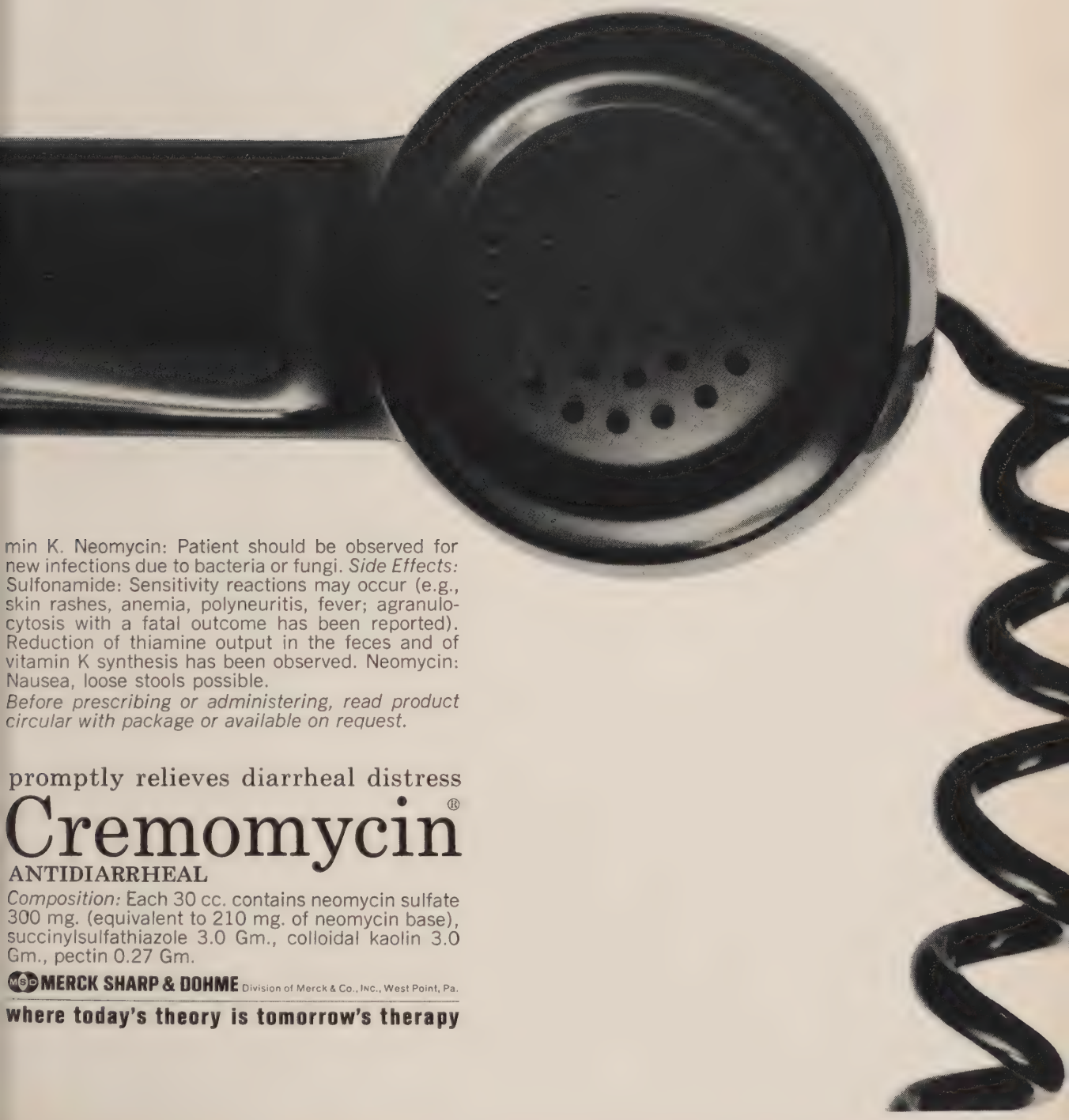


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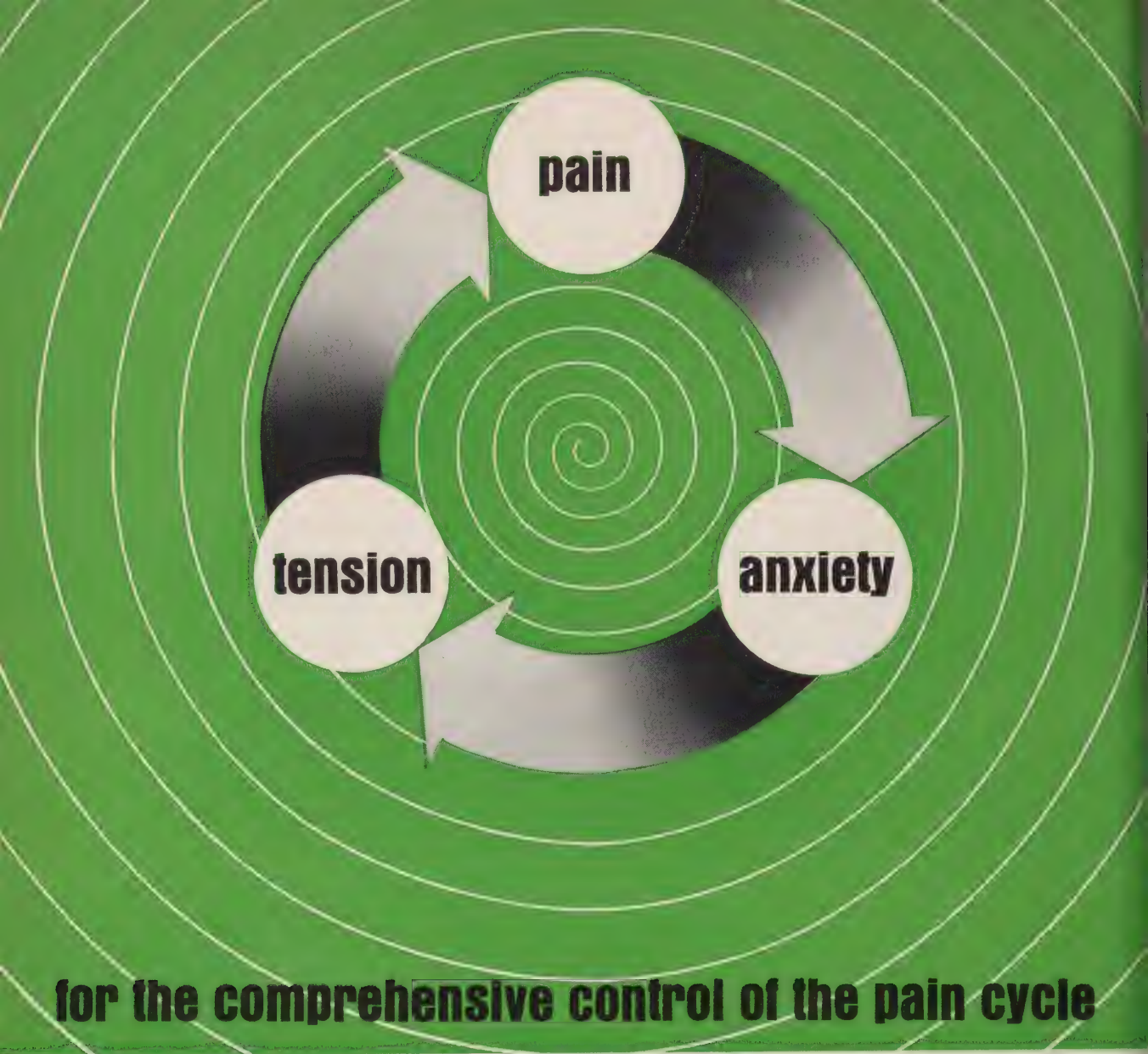
Articles and features to be found in the next issue of THE JOURNAL-LANCET

The University of Minnesota Medical School class of 1887 was evenly split between the sexes. One of the two graduates was Catharine A. Burnes, the first woman to earn an M.D. degree from the University. Since then 388 women have been graduated. A directory of these graduates has been prepared by Catherine Corson West, M.D., class of 1935. It is included in Dr. West's article in the January issue, "Watching Women Graduate from Medical School, University of Minnesota."

Dr. West's paper is the first of a series of papers honoring Dr. Ruth E. Boynton in recognition of her contributions to the health of the citizenry of this area. Dr. J. Arthur Myers, in his introduction to the "Ruth E. Boynton Series," pays tribute to the beneficent influence women physicians have exerted, to the quality of their work, and to the brilliance of their accomplishments. Appropriately, all of the authors of the articles in the series are women.

Also in January, Dr. Kenneth J. Johnson of Bismarck, whose article "Fifty Ways To Diagnose Allergy" inaugurated the "Series on Allergy for the Practitioner" in the August issue, writes on "The Relation of Cancer to Allergy." Dr. Johnson bases his paper on an investigation of 1,000 cancer patients seen at the Quain and Ramstad Clinic. One of his observations is that cancer patients have fewer allergies than noncancerous patients.

Dr. George C. Flora and Dr. A. B. Baker, both of the Division of Neurology at the University of Minnesota, collaborate on an article entitled, "The Confused Patient." This paper is one of the continuing "Series on Neurology for the Practitioner." Dr. Baker is director of the Division of Neurology.



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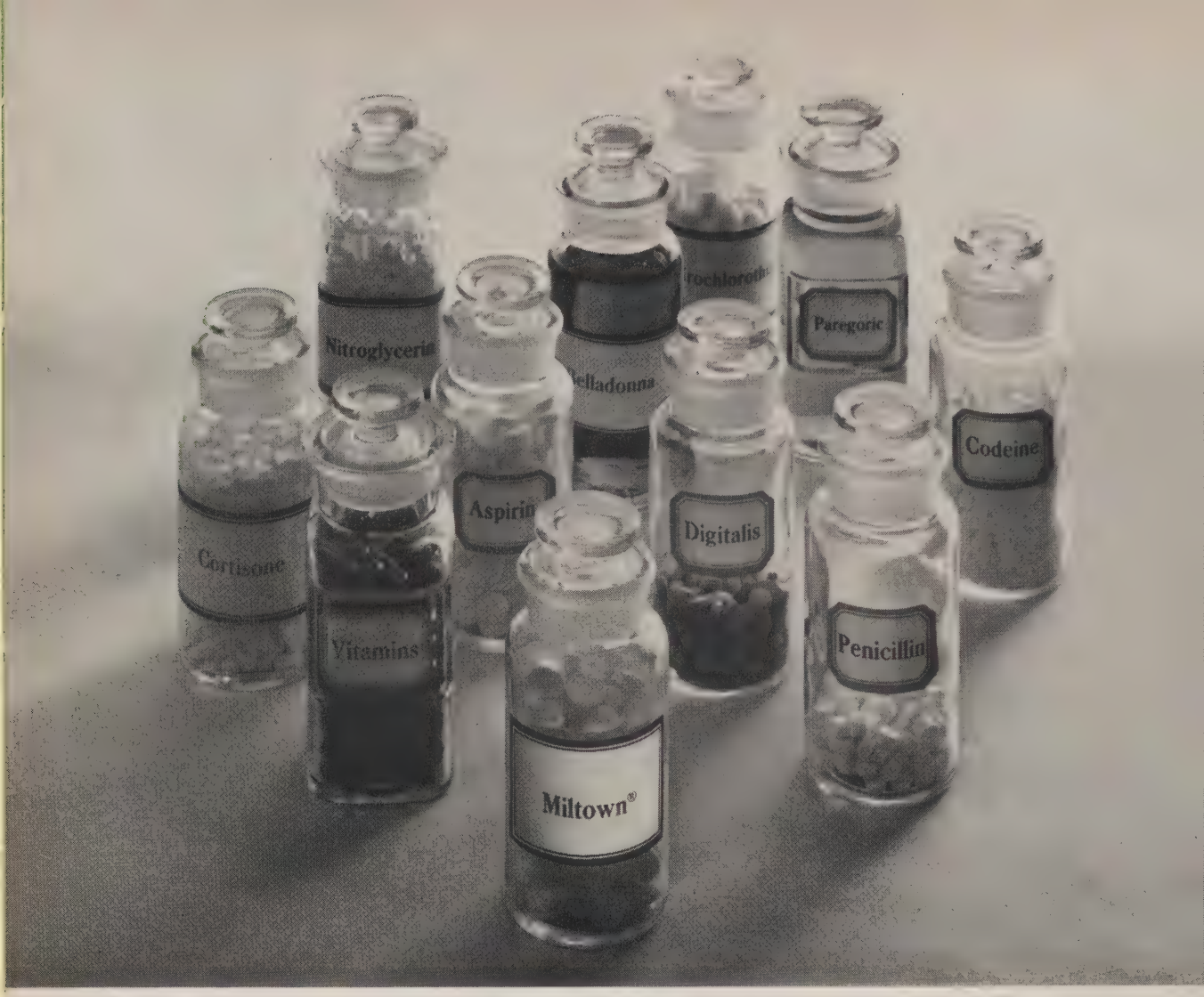
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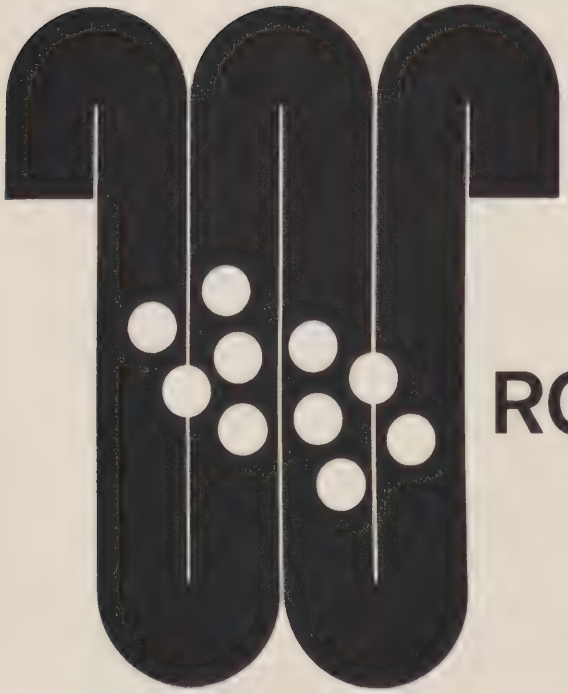


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SERVES THE MEDICAL PROFESSION OF THE UPPER MIDWEST

Series on CARDIOVASCULAR DISEASE *for the* PRACTITIONER

Instrumentation in a Catheterization Laboratory

WILLIAM F. MAZZITELLO, M.D.

Minneapolis

THE CARDIAC CATHETERIZATION LABORATORY is fundamentally a diagnostic unit wherein specialized equipment and procedures are utilized for the purpose of determining multiple physiological data relating to cardiac function. The information obtained is evaluated comprehensively in relation to the clinical findings and a specific diagnosis of cardiac disease is thus made. The instrumentation in such a laboratory is variable in its total composite makeup depending upon the specific objectives of the laboratory and the professional skills and abilities of the cardiologist. Since the initial catheterization studies by Andre Cournand and his group, remarkable changes of a progressive nature have taken place, both in the overall equipment of such a laboratory and the specific diagnostic techniques. Increasing strides in cardiac surgery have stimulated such changes and it is certain that many more developments will take place in the future.

In attempting to describe the overall instrumentation of a cardiac laboratory, this paper will touch on the general features of the equipment with no attempt to delve into the specifics of the individual electronic devices. In conjunction with this thought, the individual types of equipment will be classified and described under a definite general heading.

WILLIAM F. MAZZITELLO *is director of the Cardiac Catheterization Laboratory, St. Mary's Hospital, Minneapolis.*

X-RAY EQUIPMENT

Routine fluoroscopy utilizing spot film device for selective films was, in general, the standard equipment in most laboratories. The image intensifier has almost universally replaced standard fluoroscopy in that considerably less milliamperage is used, plus the fact that 4,000 times more intensification is achieved. The procedure can also be carried out in a lighted room with no need for accommodation for the operator and more latitude in regard to the time of the actual fluoroscopy.

In conjunction with the image intensifier, an Arriflex camera or any other suitable make, may be mounted for cineradiography. The camera permits the operator to record with the injected contrast material the actual physiological movements of cardiovascular structures with sharp clarity at rates up to 60 frames per second. Thus, on projection of the exposed film, an actual movie is made of the physiological function of the cardiac structures and adjacent great vessels. This procedure is thus utilized for detection of intracardiac shunts as well as for abnormalities of valvular function and anatomical changes of the heart chambers proper. This technique embraces ventriculography, retrograde aortography, and coronary arteriography, as well as selective angiocardiography.

The Schonander apparatus is a rapid film changer which can be used in the above procedures as a single or biplane technique. Usually

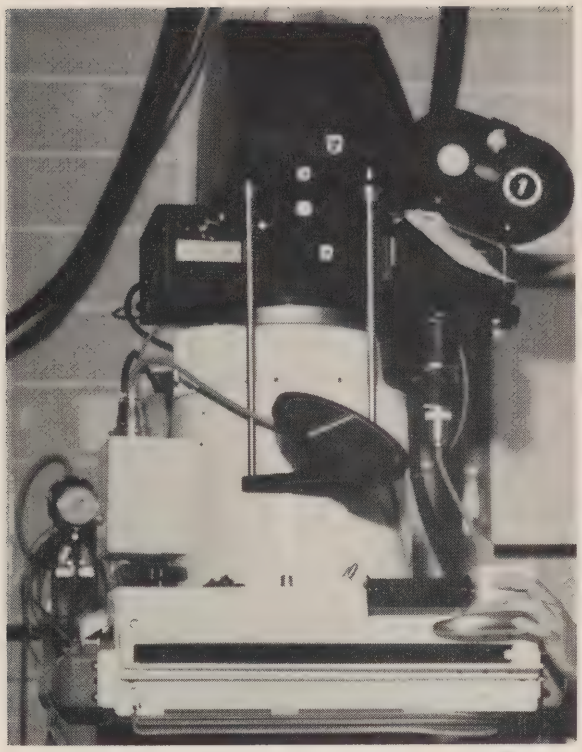


Fig. 1. Image intensifier with cine camera attached. This combination has added marked versatility in diagnostic evaluation of cardiac disease.

6 to 8 films per second are exposed and clear, and detailed anatomical characteristics of cardiac and great vessels structures are obtained. Permanent records are also obtained.

Utilization of the above rapid filming device for the highest degree of results makes mandatory the rapid injection of the contrast materials. Thus, various pressure injectors are available today for this purpose. One of the simplest to use, yet one of the best, is the Amplatz injector. This utilizes the principle of a CO_2 gas cylinder as the propellant of the contrast media. The total injection period should take only a few seconds for desired results to be obtained.

The progressive development of cardiac diagnostic techniques made mandatory certain changes in the X-ray table itself. At the present time specific tables are made for cardiac laboratories. These feature sliding table tops as well as tilt features in conjunction with certain accessory attachments which are specifically machined for ancillary laboratory instruments. These tables are specifically designed and constructed to operate with an image intensification unit.

Closed circuit television projection is also a desirable feature and has a particular place in teaching facilities so that multiple vision of the actual diagnostic procedure can be obtained. A television screen may be actually set up in the laboratory itself or projected into a conference or study room. Many potential variations exist in regard to the above.

Recently stereo image intensification with cine radiography was introduced and promises to be one of the most valuable developmental techniques for the study and diagnosis of cardiac diseases.

RECORDING EQUIPMENT

One of the most remarkable and valuable developments to have taken place in the field of cardiovascular study has been in recording equipment. Early in the developmental period of a cardiac laboratory, a twin channel Sanborn was in general use, with a DC amplifier and an electrocardiographic channel being the constituents. Increasingly improved techniques of heart catheterization made mandatory the recording of more than one pressure and other associated physiological phenomena. Thus, today one may have a choice of many and varied multichannel recording equipment with 4 to 8 channels being most common. This means that multiple pressure phenomena may be recorded simultaneously with phonocardiograms, electrocardiograms, and so forth. These recorders may be of either the direct writing or photographic type. Oscilloscopic monitoring is present on all the recent recorders so that various phenomena may be visually evaluated during the actual catheterization. The electronic potentialities that exist with these recorders are numerous, in that oximetry, cardio-green dye curves, cardiac outputs, electroencephalographic tracings, and so forth, may be

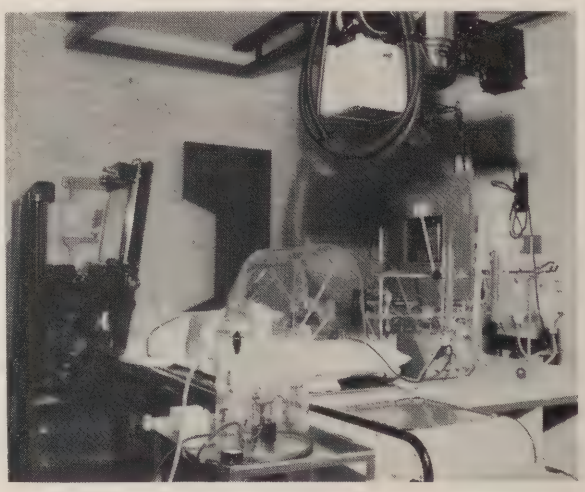


Fig. 2. The collecting chamber and hood apparatus for utilization of methyl iodide gas in detection of intracardiac shunts. A single plane schonander is seen in foreground.

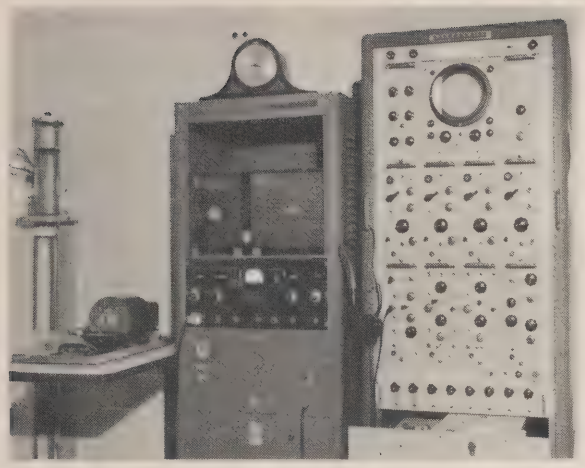


Fig. 3. A combination setup with single and double scale oximetry and a eight-channel photographic recorder for permanent records of physiological data. Dye dilution curves are done with ease utilizing this combination.

recorded as well. The more popular types of recorders are the Sanborn 550 or 560 series, Electronics for Medicine, Cambridge, Honeywell, and Waters. In the newest approach to the recording of physiological phenomena, various types of tape recording instruments have been developed with 7 to 14 channels available. These have a capacity of recording eight and one-half hours of data on a single reel of tape. This data can be played back graphically on an oscilloscope, scope, or processed by a computer.

In the latter, reference can be made to the development and utilization in cardiac laboratories of the digital and analog computers for the processing of multiple simultaneous data. This is a relatively new development and at present is not an essential part of the necessary instrumentation of a cardiac catheterization laboratory. The details of these computer systems are too complex for the scope of this paper, but may be obtained from the numerous articles which have recently appeared in the medical literature.

Vector cardiography has now assumed an integral role in the cardiac diagnostic laboratory. The record is obtained with a cathode ray oscilloscope in which horizontal and vertical deflections correspond to 2 electrocardiographic leads. Thus, from a predetermined number and positioned electrodes, electrical activity is delivered to the input amplifier channel of any recording apparatus and transmitted to an oscilloscopic screen. The visualized instantaneous loops may be photographed with a Polaroid camera and permanent records obtained.

In relation to the above discussion, it would be only in proper order to mention electrocardiography. The instrumentation here varies widely with the particular needs and objectives of the respective laboratory. In general, direct writing electrocardiograms are principally used; however, as indicated above, many recording instruments have photographic electrocardiographic recordings.

Radiotelemetry, or simply the transmission of an electrocardiogram by means of radio waves, is used in selected specific circumstances, but at this time does not appear to have a useful practical role in the cardiac catheterization laboratory. This would also apply to telephonic transmission of an electrocardiogram.

Single and double scale oximetry, as developed and utilized by Dr. Earl Wood and associates, has been an extremely valuable instrument in the diagnostic cardiac laboratory. By means of cuvette oximetry, alteration of red cell output as reflected into the calibrated galvanometer system provides immediate information as to oxygen saturation. The double scale operates by the determination of the logarithmic ratio of the red and infrared cell outputs on the calibrated scale

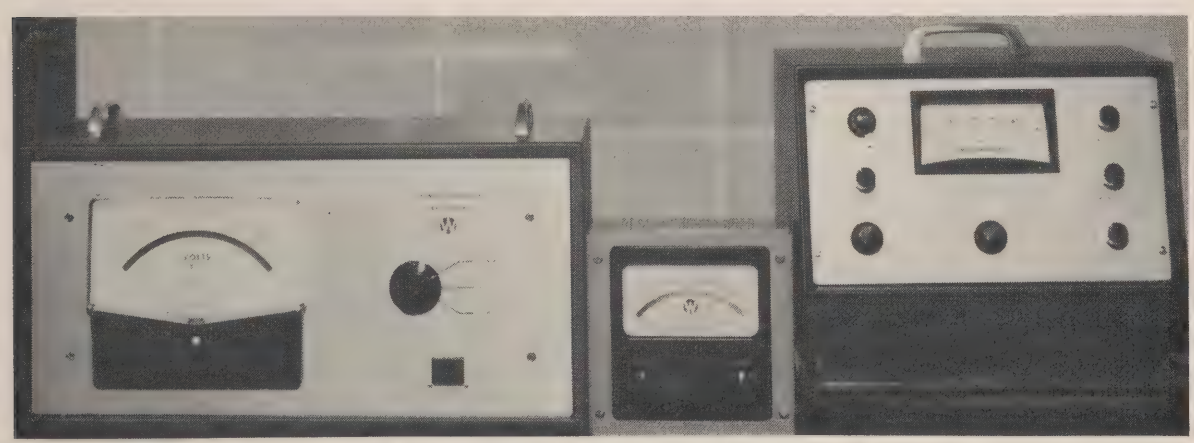


Fig. 4. Cardiac output apparatus as illustrated above. Output is thus determined by computer on right utilizing cardio-green dye curves.

predetermined and plotted by Van Slyke's analysis of blood samples. Cardio-green dye curves may also be done utilizing the cuvette and single scale galvanometer with relaying of the signal into a DC amplifying channel of any recorder. With certain electronic modifications, a densitomer, computer, and cuvette may be utilized in the determination of cardiac output, by the inpection, centrally, of known concentrations of cardio-green dye.

CARDIAC EMERGENCIES

It is imperative that equipment be immediately available for treatment of any sudden serious cardiac arrhythmia or actual cardiac arrest. The increased advances in the types of cardiac investigative procedures, especially catheterization of the left side of the heart and coronary arteriography as well as ventriculography and aortography, have increased the actual and potential occurrences of various significant cardiac arrhythmias. These are usually very transitory and are abolished by simply repositioning the catheter in the cardiac chamber.

The defibrillator commonly utilized was an AC type and could be applied for either open or closed-chest defibrillation. This type was not particularly advocated, however, for utilization in the termination of arrhythmias such as ventricular tachycardia, auricular fibrillation, or auricular flutter.

The recently developed and clinically proved DC instrumentation for the termination of either auricular or ventricular arrhythmias, as well as cardiac arrest, has changed the morbidity of these events considerably. The Lown cardioverter, for example, has complete monitoring, pacemaking, and internal or external defibrillatory and cardioversion features which have made it one of the most acceptable. Many other good cardioverters with the above features are now available. The essential feature is the absolute necessity of having the instrument at all times in the cardiac laboratory for immediate utilization if the need arises. The safety features of these instruments have been well proved.

MISCELLANEOUS INFORMATION

1. Pressure transducers are of various types and designs with certain fundamental differences in their characteristics. The most commonly used transducers are those manufactured by the Statham Instrument, Inc., and are of 5 different models, dependent upon volume displacement and frequency response. The basic principle is that of a Wheatstone bridge. Recently Statham has introduced transducers so small they can be mounted on the catheter tip.

Variable inductance transducers are also produced so that alterations in the single or multiple catheter types will produce a signal or differential output as regards pressure measurements.

2. Determination of pO_2, pCO_2, and pH are in essence part of the diagnostic armamentarium of a laboratory. The pO_2, or partial pressure of oxygen in the blood samples, may be interposed with the oxygen saturation. The pCO_2 is also helpful in the evaluation of partial pressure of carbon dioxide with pulmonary parenchymal diseases being ruled in or out as primary factors. The pH determinations also correlate closely with the above determinations of pO_2 and pCO_2. These data are extremely important in the treatment of variably induced cardiac disease states.

METHYL IODIDE

The utilization of radioactive gases for the detection of very small intracardiac shunts has been extremely valuable since this type of cardiac defect can be easily missed by Van Slyke sampling, oximetry, or pO_2 sampling. Krypton is another gaseous substance which when made radioactive has been extremely valuable for this purpose. The essential principle in methyl iodide inhalation is the passage of the radioactive gas after inhalation from the alveolar compartments into the capillary blood of the lungs and then to the pulmonary veins and left side of the heart. The presence of an intracardiac septal defect would permit the passage of this gas to the right heart chambers and thus would be picked up by continuous sampling via a right heart catheter. The samples thus obtained from the respective heart chambers are evaluated as to their radioactivity, and curves thus plotted will identify the presence or absence of intracardiac shunts and the exact site if a shunt is detected.

SUMMARY

An attempt to delineate in an uncomplicated manner present day instrumentation in a cardiac catheterization laboratory has been made. Understandably, no two laboratories will be in agreement as regards specific types of equipment or the interrelationships of usage that potentially exist with the available equipment. Also, with numerous new developments in medical electronics, it would be impossible to deal with all in any degree of completeness. Such a task would definitely be beyond the scope of this paper. It is hoped that the reader will have a greater comprehension of what is involved in regard to the overall instrumentation present in a cardiac catheterization laboratory, since this paper was essentially directed to those not familiar with the equipment or operations of such a laboratory.

Inhalant Allergies with Headache as the only Symptom

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HEADACHE is perhaps the commonest abnormal sensation that human beings experience. Because of the erroneous but widespread belief among many people, including not a few of our medical confreres, that most headaches are due to affections of the nose or paranasal sinuses, a large number of these sufferers eventually find their way to the otolaryngologist. Early in my practice of otolaryngology, I was repeatedly confronted by patients with headache problems who came for evaluation of the nose and paranasal structures as the possible cause of their discomfort. It was not uncommon after the examination to decide that the pain the individual was experiencing was not due to abnormalities in his sinuses or nose and to either recommend a return to the physician who had referred him or to dismiss him without a suggestion as to where next he should seek relief. In consequence, the patient then drifted to the ophthalmologist, the neurologist, and the dentist. In spite of having been relieved of a deviated septum and a few teeth, fitted with the latest in eyeglasses, fed a variety of different analgesics, and advised to reorganize his life, he concluded his peregrinations with his headache still intact. By then he was ready to accept discomfort as inescapable. I soon became dissatisfied with this course of events and embarked on a project of inquiry into the problem of headaches.

It has only been in recent years that the subject of headaches has become of increasing interest. Now the otolaryngologist, as well as other practitioners of medicine, should be well-informed as to the vagaries and vicissitudes in the diagnosis of such a problem. Except for an occasional paper, little attention has been paid to one aspect of the problem—inhalant allergies. This is the topic that I shall discuss as related to headache. Although it is not one of the usual etiological factors, at times it is very important. The type of headache that I will delve into is the headache due to inhalant allergies with practically no other allergic symptoms.

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CLASSIFICATION OF HEADACHES

To approach the headache problem rationally, one must have an understanding of the various etiological possibilities. Many classifications have been proposed from time to time, but recently they have been logically separated into 2 distinct groups: (1) vascular and (2) nonvascular. The following classification has been modified from the one proposed by Hansel[1] and Ouer.[2]

- Vascular
  - Allergies
    - Foods
    - Inhalants
      - Dust, molds, pollens, etc.
      - Osmyls (perfume, etc.)
    - Endocrines (ovaries, etc.)
  - Migrainous types
    - Classical migraine
    - Migraine variants
      - Ophthalmic
      - Ophthalmoplegic
      - Status migrainous
      - Abdominal
  - Tension
  - Histaminic cephalgia (Horton)
    - Typical
    - Atypical
  - Hypertension
  - Arteritis (temporal, etc.)

Nonvascular
- Intracranial
  - Meningeal irritation (meningitis, hemorrhage, syphilis, etc.)
  - Lesions producing pressure (tumors, abscesses, hematomas, etc.)
  - Postlumbar puncture
- Nasal or paranasal sinus
  - Sinusitis (infection and allergy or both)
  - Structural abnormalities (septal spurs, etc.)
- Otitic
- Ocular
- Neuralgic (trigeminal, glossopharyngeal, etc.)
- Pyrexic, toxic, uremic
- Psychogenic
- Endocrine
  - Thyroid (hypo- or hyper)
  - Others
- Posttraumatic
- Myalgic (cervical)
- Hypoglycemic
- From temporomandibular-joint syndrome (Costen)
- Oral (dental, etc.)
- Osseous (from arthritis, disks, etc.)

The possibility that a specific hypersensitivity can produce headache has been recognized for many years, and most observations have been directed to the etiological relationship of these sensitivities in production of migraine. In 1931 Eyermann[3] described a group of headaches that did not correspond to the recognized migraine pattern in that the preceding cortical features were replaced by nasal blockage and mucoid discharge; the pain was frequently frontal, diffuse, or bilateral; and there was a following, or often accompanying, abdominal discomfort and nausea, with or without vomiting. He noted a high incidence of food sensitivity and also found positive reactions to inhalants. In 2 patients he felt that the headache had been induced by exposure to inhalants as well as to foods. Instead of allergic migraine, he proposed the term "allergic headache" as the proper designation for this syndrome. In 1932 Rinkel and Balyeat[4] confirmed Eyermann's observations.

Also in 1932, Goltman[5] reported a series of unusual cases of migraine in which skin reactions were positive to certain inhalants such as pollens, orris root, and animal hairs. Satisfactory relief from the headaches was not obtained until the patients had been hyposensitized to the inhalant sensitivities. In 1933 Forman[6] recorded a similar series of cases, and Sheldon and Randolph[7] did the same in 1935. For a number of years thereafter, the literature was barren of such reports, and the subject was not revived until quite recently, when the mechanisms of various headaches became more clearly defined.

I agree with Shuey[8] that one would experience great difficulty in immediately classifying any given headache as an allergic cephalalgia solely on the basis of the history that the patient recites. Since there is usually nothing typical of such cases, there are no characteristic pain patterns. Kern[9] recently said, "The central nervous system provides one of the commonest of allergic symptoms: headache. Allergic headaches are of the most varied kinds, ranging from a dull generalized ache to the severest migraine." Many observers have stressed that in the beginning, at least, the pain has a frontal location. At first it centers over either eye, or occasionally in the occipital region. Later, it may become generalized over the entire head. The severity of the headache is often proportional to the amount of contact the patient has had with the offending allergen.[10]

Davison,[11] in a study of a large number of cases of cerebral allergy, found that the commonest cause was food allergy, although some were due to inhalants such as dust, and a few were due to the inhalation of food odors, particularly onions or cabbage. The outstanding symptoms were sleepiness, mental retardation, and confusion. In the past, several authors have stressed the important fact that fatigue is one of the foremost symptoms of food allergies. It could readily be an expression of the cerebral effect of the allergy, as Davison has noted. On careful questioning and observation, many individuals with the fatigue syndrome have been found to be suffering from headaches, among other things. Therefore, the probability of an allergy looms large in an individual with headache and fatigue.

The characteristics of the onset of the headache may provide a clue to an allergic etiology. Hansel[1] states that the onset is usually gradual, since the mechanism of the allergic headache is not based on a vasoconstrictor-vasodilator action but on capillary permeability and edema. In addition, there are several other characteristics that may direct one's attention toward an allergic etiology. These are (1) a personal history of allergic disturbances such as eczema, angioedema, urticaria, and allergic rhinitis, (2) a strong family history of allergies, and (3) concomitant allergies such as seasonal and perennial rhinitis and urticaria.

After one's suspicions have been aroused, it is well to remember that foods are more likely to produce cerebral reactions than inhalants are. Thus, foods should be considered first. Milk, wheat, egg, chocolate, nuts, pork, and coffee are perhaps the most important.

Several etiologic types of allergic headache

have been mentioned, but there are no characteristics by which they can be readily differentiated. The specific diagnosis must wait upon a determination of the degree of severity of exposure to specific allergens, the allergic load that is present at the time of examination, the location of the allergic reaction in and around the head, and the nature of the reaction—whether it is vasodilation, edema, or something else.

However, the frontal type of allergic headache, which has been very well discussed by Ogden,[12,13] has been the most frequent in my experience. Ogden describes a syndrome of frontal pain which is present in a large percentage of patients with respiratory allergy. The pains are usually bilateral, they may appear in the absence of definite nasal symptoms, and they may last from an hour to several days. Because the pain may also appear in the vertex, occipital regions, and face, it may coexist with other headache patterns. An inhalant antigen or histamine, released as a part of the allergic reaction, Ogden thinks, could produce pain through its vasodilating effect upon a sensitized artery.

The involved vessels are probably the anterior and posterior ethmoidal arteries and their branches. These arise from the ophthalmic—a branch of the internal carotid—as it courses forward along the medial wall of the orbit. They pass medially between the superior oblique and medial rectus muscles. The posterior ethmoidal, which is the smaller of the two, traverses the posterior ethmoidal canal and supplies the posterior ethmoid sinuses and the posterior upper part of the lateral wall of the nasal cavity. The anterior ethmoid passes through the anterior ethmoidal canal with the anterior ethmoid nerve and enters the anterior fossa of the skull, crossing the cribriform plate of the ethmoid through the nasal slit. In its course in the anterior cranial fossa, it gives off anterior meningeal branches. Passing laterally to the slit, it enters the nasal cavity where it descends on the inner surface of the nasal bone and continues on to the nasal tip and supplies the anterior and middle ethmoid cells, frontal sinus, and skin of the dorsum of the nose. Ogden postulates that the vessels involved are probably not the anterior and posterior ethmoidals, but pressure exerted on them by tissue edema, produced by an allergic reaction, may trigger the mechanism which secondarily involves the meningeal branches of the anterior ethmoidal artery or other branches of the ophthalmic. This presumption is based on the fact that pain impulses which arise in the nasal cavity are usually not referred to the frontal area. Also, since the anterior ethmoidals supply the frontal sinus, it is logical to suppose that these frontal sinus branches may possibly be involved in producing frontal sinus pain with sinus involvement per se. Since pain relief can frequently be secured with the use of vasoconstrictor drugs such as the ergotamines, it is generally felt that this is a distinct type of vasodilating headache. Others,[14] however, have felt that the site of pain was at the ostia of the sinuses (the interior of the sinuses being relatively insensitive to pain) and have thought that localized mucosal edema is responsible for the discomfort.

The pathological phenomena that occur in headaches are many and varied. The well-known work of Wolff and his collaborators[15] was the first great contribution to our understanding of the physiopathology of head pain. Since then, several outstanding studies have appeared, especially those of Hilger, who linked autonomic imbalance with vascular phenomena. Still others[16,17,18] have added considerably to our knowledge of the effect of allergic response upon the vascular and other tissue systems. A complete discussion of this aspect is not within the scope of this presentation.

NASAL CHARACTERISTICS OF A FRONTAL ALLERGIC HEADACHE

There have been various opinions advanced by several authors as to the prevalence of nasal symptoms observed in patients with an inhalant allergy headache. Several have stated that symptoms of an allergic rhinitis with its discharge and blockage are seen in a large majority of patients, while others have been of the opposite opinion. This discrepancy in observation probably stems from a different evaluation of the pain as described by the patient. Since the evaluation can only be subjective, discrepancies can exist. Almost all cases of allergic rhinitis, if severe enough, will have some degree of low-grade frontal headache. The greatest complaint, however, is the airway blockage and only on direct questioning do they mention headache. However, the patient who presents himself with only frontal headache and almost complete absence of nasal symptoms, I feel, experiences a different type and degree of head pain—his being more severe. Often, if he does have any nasal symptoms they are lost in the haze of his discomfort. Since the headache of an allergic rhinitis is due to pressure on sensory nerves in the nose from the edema of the tissues and since the frontal headache under discussion is probably of a vasodilating type, the difference in severity becomes apparent. Therefore, when confronted with a problem of a frontal headache of varying severity

with few nasal symptoms, it is well to think of an allergic headache.

DIAGNOSIS

Diagnosis of inhalant allergic headache is made by (1) never-ending suspicion of an allergic etiology behind every functional headache, (2) detailed and accurate history, (3) identification of the allergen by history and skin tests, and (4) relief of symptoms consequent to specific avoidance or hyposensitization, or both. I cannot overemphasize the advantages of a good history. Taking a satisfactory one requires time and patience. It is not a job that a harried examiner can accomplish. Several sessions of questioning may be necessary, for, in addition to providing invaluable information, the interviews can have a distinct and valuable psychological effect upon the patient. He is reassured, and thus relaxed, for at last he feels that he has found someone who is really interested in his plight. I find that any of the headache-history outlines can be a time-saver and an aid to accuracy. Skin tests are invaluable aids at times but one must be cognizant of their limitations. Negative results do not rule out a possible allergy, nor do positive results prove that one is present.

Since foods are known to produce headache, a thorough investigation of this possibility is essential. I would be presumptuous to detail the several methods of assaying this problem since many of you have had much more experience than I in the diagnosis of food sensitivities. All of us will agree that many times foods present quite a problem in diagnosis. I place little reliance on specific skin tests but such testing at times may give us valuable leads. In my limited experience I have found the abstinence–refeeding procedures as outlined by Rinkel, Randolph, and Zeller,[19] are helpful at times but are time-consuming. The elimination diets which have so carefully been worked out by Rowe[20] are much easier to use and offer an excellent approach in bringing to light the allergenic foods. The so-called "cereal-free" diet is quite easy to use. In addition, I remove milk, eggs, cheese, fish, fresh fruits, chocolate, nuts, spices, and coffee. With this diet almost all foods that might prove to be etiologically significant are eliminated. Food diaries have not proved to be of much value in my experience except when a rarely ingested food is the offender. If one accepts the concept of the dynamic nature of food allergy with its various phases of sensitization such as hypersensitivity, latent sensitization, and masked sensitization, it is obvious that such a diary is of little usefulness. Recently,[21] the so-called "provocative test" has been advocated. This test is described as a deliberate intracutaneous injection of a potent food extract of sufficient quantity and strength to produce the accepted allergic symptoms. The test is based on the phenomena by which symptoms produced are immediately relieved by the injection of weaker solutions of the antigen. This method, although it may prove to be accurate, is quite technical. I have had only limited experience in its application. Examination of nasal and pharyngeal smears for eosinophiles may be helpful, as is examination of blood smears.

The recent informative monograph by Randolph concerning the production of, or triggering of, allergic reactions by the inhalation of unsaturated hydrocarbons of household natural and bottled gas, should make us aware of this possibility. I have several patients whose frontal headaches have been relieved by locating a leak in their heating plant, gas water heater, or kitchen stove.

It is well to look for a subclinical hypothyroidism, as Jones[22] and Proetz[23] have pointed out. The basal metabolic rate is frequently normal, but abnormal values may be found for blood cholesterol and protein-bound iodine. Other diagnostic features are a subnormal afternoon temperature and a slow pulse.

Since headache is no more than a symptom and can be evaluated only subjectively, the diagnosis of an allergic etiology must be made by inference and confirmed by specific avoidance, provocative testing, and hyposensitization.

TREATMENT

The ideal treatment for the inhalant allergy is, if possible, elimination or avoidance of the offending allergen. Again, I wish to repeat that one should remember the osmyl factors that may be causative. However, in many instances, neither avoidance or elimination is feasible or possible so hyposensitization becomes necessary. Other concomitant sensitivities, especially food allergies, must be sought out. In regard to food sensitivities, I have stumbled on an interesting fact about grapefruit. I have had several patients with nasal symptoms and headaches, or both, which have appeared only during the fall, winter, and spring. One would conclude that the most probable offender would be house dust. However, this is also the grapefruit season—grapefruit being absent from the market or very expensive during the summer months.

Since the type of headache under discussion is probably vascular in nature it would follow the course of other vascular headaches in that there

would be (1) an acute attack or preedema phase which is the time of vessel dilation and (2) a vessel edema phase. I will not elucidate on this course of events since I am sure this is well known to all of you.

THE PREEDEMA OR VASODILATING PHASE OF THE ACUTE ATTACK

Arterial constrictors are of definite value in this phase. Epinephrine 1:1,000, in doses of 0.25 to 0.5 cc., may abort the attack. More reliable therapy is the use of ergotamines. Dihydroergotamine methanesulfonate (D.H.E.45®) may occasionally be necessary in doses of 0.5 to 1 cc. Cafergot P-B is useful but the dosage level employed must be tailored to the patient. The recommended dosage is 1 tablet at half-hour intervals to the point of relief, but not exceeding 6 tablets. However, I have had better results by raising the initial dose to 2 or 3 tablets. In some patients the oral route is not feasible because of gastric discomfort produced by the drug, so rectal administration is necessary. A convenient form is the cafergot P-B suppository or similar medications.

THE EDEMA STAGE OF THE ACUTE ATTACK

In this phase the preceding measures are usually ineffective. I have found that calcium gluconogalactogluconate (Neo-Calglucon®), 20%, given intraveneously in 10 cc. doses is helpful. Three cubic centimeters are injected rapidly, followed by a pause until the flushing fades; then another 3 cc. are given, and another wait for the flushing to subside; and then the final 4 cc. are given.[24] At times, sedation and analgesics are indicated since there are some individuals in whom, for various reasons, allergic management fails to produce the desired relief. Other supplemental measures are useful. Antihistamines may be of benefit until adequate allergic management can be obtained. Small doses of thyroid extract may prove effective and large doses of ascorbic acid will have some action in preventing tissue edema.

According to the concept that autonomic imbalance is probably a basic factor in vasodilating headaches, one may include the use of Bellergal® a combination of ergotamine tartrate—a sympathetic inhibitor, Bellafoline®—a parasympathetic inhibitor, and phenobarbital. Prochlorperazine (Compazine®) at times is of benefit, as is the rauwolfia series of drugs.

Corticosteroids are useful in those patients with allergic headache who have failed to respond to all types of medication when the cause cannot be ascertained at the moment or when the situation is desperate.

CONCLUSIONS

An allergic basis should be considered in the evaluation of any functional headache. Headaches, at times, may be produced by an allergic reaction to a specific inhalant allergen. The diagnosis of an allergic etiology must be made by inference and confirmed by specific avoidance therapy, provocative testing, and hyposensitization. Some of the unsatisfactory results in the treatment of headache no doubt reflect a failure to recognize the presence of inhalant allergies.

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JAMES J. WARING *Series*

Experimental Hemorrhage

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ONE OF THE MOST COMMON acute physiological insults occurring in man is hemorrhage. If sufficiently rapid and of adequate magnitude, hemorrhage, as such, is uniformly lethal. If of lesser magnitude or more prolonged, it may initiate a recognizable syndrome of body responses that have been termed "hypovolemic shock." Unfortunately, "shocklike" states are the result of a multiplicity of stresses, and, also unfortunately, shocklike states in which hemorrhage plays a part usually are associated with other factors such as tissue trauma, body exposure, or psychic turmoil. An excited, frightened soldier had a shell fragment wound of the buttock which severely damaged the muscle masses, perforated the rectum, and cut the hypogastric artery. He lay in a cold rain for two hours before being carried into the aid station. A girl in an automobile had both legs fractured, a concussion, and a bleeding spleen. Even the man attempting suicide was emotionally taut for hours before he slashed his wrists. Pure hemorrhage is, indeed, a rare cause of shock, but it is present in so many situations as one of the components of trauma that an understanding of the body's response to hemorrhage and of the mechanisms activated to restore biologic integrity is important.

An experimental model should be available to study hemorrhage alone, which is sufficiently standardized so that it will generate highly reproducible data and, at the same time, is sufficiently similar in its responses to man so that the results will be meaningful in the understanding of clinical hemorrhage.

For a long time it was thought that such a model did exist in the Wiggers-Fine method of prolonged hypovolemic hypotension in the dog. In this experiment, the animal is bled arterially into a resevoir which is positioned at a level which will maintain a predetermined blood pressure, the height of the reservoir moderating the animal's blood pressure. The term "hemorrhagic shock" was loosely applied by many investigators using this method, but, unfortunately, the technique itself obtunds or ablates many or perhaps all body responses to the loss of blood. If fluid pours into the plasma in an attempt to increase circulating volume, it is at once bled into the reservoir. If large vein paralysis occurs and blood is pooled within the body, a transfusion is administered from the bottle. Obviously, the model is of no value in the study of hemorrhage, since it washes out some of the very responses one would like to examine. In the Wiggers-Fine preparation, the blood pressure is the parameter which is manipulated and maintained at a predetermined level. The blood volume and fluid spaces and their disposition will vary, but the blood pressure remains in a stable hypotensive state for a specific period of time. I presume the observations that have been made on this model are pertinent to the effects of prolonged oligemic hypotension. They should be recognized for what they are and the term "hemorrhagic shock," meaning a state of shock induced by a hemorrhage alone, should not be used.

For these reasons about ten years ago we began an investigation to develop an experimental model which could give meaningful data on the mechanisms involved in an animal in response to a specific rapid loss of blood volume.

The experimental animal. The dog is the animal most commonly available for surgical research. It is by no means clear, however, that it is the best animal for the study of shock if the results are to be applied to man. For example, there are several known ways in which dog clearly differs from man, ways which relate to its

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TABLE 1

EFFECTS OF ANESTHETIC AGENT ON BLOOD PRESSURE AND PLASMA VOLUME CHANGES IN NORMOTHERMIC ANIMALS

	(Group 3) Pentobarbital (15 animals)	*(Group 4) Unanesthetized, morphine and barbital ether (7 animals)*
Mean prehemorrhage blood pressure (mm. Hg)	135	96
Mean blood pressure fall (mm. Hg)	85	46
Mean plasma dilution (%)	15	9

responses to hemorrhage. To mention a few, (1) the dog has a relatively larger spleen that can relax or contract, thus causing major changes in blood volume, (2) the dog has a sphincterlike mechanism in the outflow tract of the liver which results in liver congestion under certain conditions and thus disturbs many homeostatic mechanisms, (3) the dog carries viable anaerobic organisms in the liver parenchyma that become active during hypotensive or oligemic conditions, (4) the transport of fluid across space barriers in the dog is extraordinarily rapid, and (5) the dog suffers from endemic hemobartonella infection which causes a large percentage of the canine population to be anemic.

However, because the dog is the right size, relatively cheap, and abundantly available, and because no other animal is known to be better for the purpose, the dog was used in these studies after being modified by splenectomy so that a more constant blood volume could be obtained and the complexities of various sized autotransfusions could be avoided. In addition, hematocrit was measured before use and, if it proved to be low, the animal was barred from the study. Thus, difficulties, Nos. 1 and 5 in the list above, were avoided. A comparison of the responses in a variety of physiological parameters between man and many other species of small animals should be made, however, to attempt to find a better subject for the experimental model of hemorrhage.

Every animal used weighed between 15 and 30 kg., was in apparent good health, was inoculated for distemper, and was observed in the kennel for at least one week. After a hematocrit had revealed no anemia, splenectomy was performed using pentothal anesthesia. The dog was then allowed to recover from the operation for a period of one month or more, so that we would not be studying an animal with recent trauma but, rather, one that was leading a stable, healthy life. After maintaining weight and health and not becoming anemic, the dog was considered ready to serve either as an experimental or control animal in the study.

In order to assure stable conditions, to protect the animals from suffering, and to minimize the variable psychic response to manipulations, it was elected to perform the experiments under anesthesia. However, it is a well-recognized fact that different anesthetic agents and levels of anesthesia have a profound effect upon the cardiovascular responses to changing blood volumes. Table 1 presents some data illustrating this point with deep ether anesthesia in dogs incapable of suppressing venous and other vascular responses to hemorrhage. Figure 1 shows the blood pressure response in an etherized dog to a standard hemorrhage which is uniformly nonlethal in a stable animal. We see that the blood pressure did not return to normal levels until the ether was discontinued, but it could not be maintained, and the animal entered a state of shock and died.

We needed a general anesthetic that could be administered easily and that had a uniform effect and with which a constant depth of anesthesia could be maintained. We finally elected to use pentobarbital, 28 mg. per kilogram of body weight intravenously, as a beginning dose. Small increments averaging 6 mg. per kilogram per hour were needed to maintain a level of narcosis in which the medial lid reflex was suppressed but the lateral one was maintained. This is a sufficiently light level of anesthesia that preserves the cardiovascular reflexes. We must admit, nonetheless, that the responses studied are those occurring in a lightly anesthetized, splenectomized dog rather than in a normal unanesthetized one. We think, however, that the

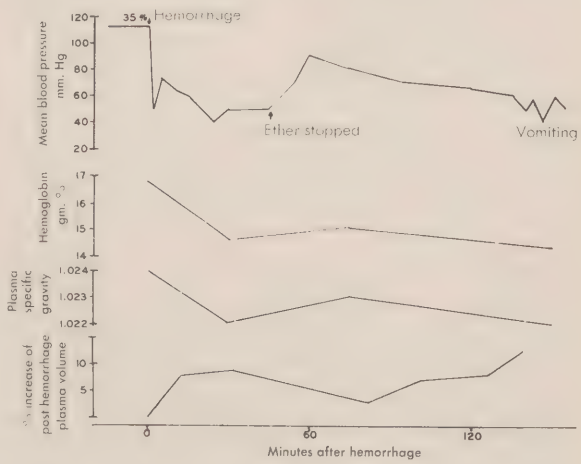


Fig. 1. Response to hemorrhage of 35% of blood volume during ether anesthesia

compromise is essential and actually will improve the reliability and enhance the applicability of the data obtained.

TECHNIQUE

Bleeding. For rapid, accurate bleeding of fairly large volumes of blood, the aorta is the best site to tap for an example of arterial hemorrhage. A large plastic cannula was inserted via one of the femoral arteries. Through this cannula 50% of the blood volume of the dog could be removed by suction in less than five minutes.

Blood volume. It has been well established that, in dogs, blood volume per unit of weight varies considerably between species and even between animals of the same species. This is also true in man, as between the sexes and between widely varying body habits. Fat people have much less blood per kilogram of total weight than thin ones and, hence, tend to tolerate hemorrhage less well. It seemed unlikely, therefore, that we would be able to obtain highly reproducible results by bleeding specific volumes per kilogram of body weight. This was confirmed by a series of animals in which larger increments of blood were withdrawn on the basis of milliliters of blood per kilogram of weight. There was no correlation between survival and the volume of blood per kilogram extracted. Indeed, there was some mortality at all levels, from 20 to 45 cc. per kilogram. It seemed more promising to measure blood volume first and then bleed a specific percentage of that volume. Thus, from animal to animal, the insult to their homeostatic mechanisms should be essentially equivalent.

Prebleeding plasma volumes were measured by means of the dilution of radioactive iodinated human serum albumin (RIHSA), as based on the ten-minute sample. This was converted to blood volume by the hematocrit determination obtained by the method of Hlad and Holmes.

One of the prime objectives of the studies planned in using this experimental model was to observe the changes in plasma and blood volume which occur as time passes following the bleeding. It is possible, of course, to use intermittent plasma determinations by repeat injections of either RIHSA or of Evans blue dye (T-1824). But this system suffers from a rapid buildup of either radioactivity or color, thus limiting the frequency of the determinations. What we needed was a method for continuously monitoring plasma (blood) volume. Since the limits of the experiment were rigidly defined, such a method could be developed, and the technique was successfully applied. It can be used in any experimental situation involving hemorrhage when (1) the only experimental change is loss of blood, (2) the volume of the hemorrhage is known, and (3) if further bleeding occurs or is deliberately induced the volume of the additional hemorrhage is known (for example, the removal of blood for sampling or a deliberate second or third bleeding). These conditions do not apply often in the clinical situation, but in the experimental laboratory the technique is a useful tool.

Some of the key steps in the evolution of this method developed in the answer to some specific questions:

Question: Are the Evans blue dye (T-1824) and the RIHSA dilution techniques equivalent?

Answer: Yes. The data supporting this conclusion are presented in table 2. In 45 dogs, the mean difference in simultaneous determinations of the plasma volume by the 2 methods was only 1.8 ± 10.2%. This allowed us to use the RIHSA indicator with considerable confidence in its accuracy.

Question: Do the 2 methods of measuring dilution, namely, the 3-point retroextrapolation and the one ten-minute sample, give equivalent results?

Answer: Yes. With a single RIHSA injection, table 3 tabulates the plasma volumes obtained as calculated by the 2 methods in 46 dogs. The equivalence is remarkable, since the mean difference was only 0.6 ± 2.5%. This enabled us to use the much simpler single sample technique with confidence.

Question: In an animal under the conditions of the experiment (a splenectomized dog lying quietly under stable thiopental sodium (Pentothal®) anesthesia), is the disappearance rate of RIHSA from the plasma relatively uniform and can it be predicted with accuracy from animal to animal?

Answer: Yes. The disappearance rate is remarkably uniform under these conditions. Figure 2 is a graph of the disappearance curves in 9 animals during the first six hours, expressed in terms of the radioactivity of the plasma as compared with the radioactivity of the ten-minute sample.

From these data, it was possible to derive a mean disappearance curve and to calculate its 99% confidence limits. This "curve" is illustrated in figure 3. It is remarkable to observe how narrow are the confidence limits using this mean disappearance curve.

Question: Will this line predict plasma radioactivity and, therefore, plasma volume at any time (at least up to three hours) after the injection of the isotope?

TABLE 2

COMPARISON OF PLASMA VOLUMES SIMULTANEOUSLY DETERMINED BY T-1824 AND RIHSA ON 43 DOGS

Mean T-1824 volume	668.4 ml.
Mean RIHSA volume	688.6 ml.
Mean difference	22.1 ± 69.8 ml. (−1.8 ± 10.2%)

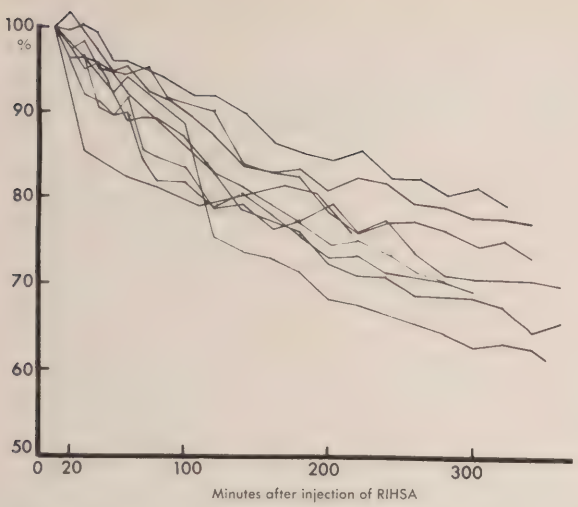


Fig. 2. Disappearance rate (%) of radioactivity of plasma RIHSA during ten-minute concentration

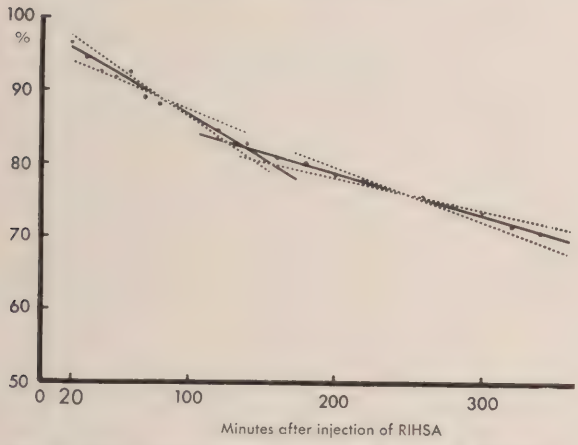


Fig. 3. Mean disappearance curve of plasma RIHSA in 9 dogs; percentage after ten-minute concentration

Answer: Yes. This hypothesis was tested by measuring the plasma volume by a second injection of RIHSA and checking the ten-minute sample volume against that predicted by extrapolation from the mean disappearance curve. This last step was performed as follows: A transparent template was constructed from the line in figure 3. The left-hand margin lay along the ordinate of the semilogarithmic paper, while the superior border followed the line. After an injection of a known amount of RIHSA, samples were drawn at ten and again at twenty minutes. The plasma volume was calculated from the ten-minute sample. The twenty-minute sample was plotted on semilogarithmic paper. The edge of the template was now appropriately positioned on this point and, where the superior border crossed the ordinate, the value was noted, and this value was used in the calculation of the initial plasma volume, just as if it had been obtained by 3-point extrapolation instead of by the mean disappearance curve template.

With this means for comparison, the initial plasma volumes in 17 dogs were determined by the 2 methods. The mean volume for the ten-minute point was 859 ml., and by extrapolation from the mean disappearance curve it was 838.2 ml. The mean difference was 9 ± 16.5 ml. (0.8 ± 2%). This compares directly with the previously demonstrated mean difference of 6.5 ± 26.8 ml. (0.6 ± 2.5%) between plasma volumes as measured with RIHSA with the ten-minute sample and with the standard extrapolation procedure (Table 3).

The predicted volumes were checked in 10 dogs by an injection of T-1824 at two hundred minutes. The mean difference was 7.3 ± 8.1 ml. (1.2 ± 6.7%). The correspondence is at least as good as when T-1824 and RIHSA are used for simultaneous direct plasma volumes (Table 2).

The predicted plasma volumes were again checked in 7 of the above 10 dogs by a second injection of RIHSA at three hundred fifty minutes. The mean difference was 8.4 ± 99 ml. (0.1 ± 4.6%). Thus, at three hours the mean disappearance curve was giving remarkably valid results.

Question: Would the mean disappearance curve also be valid when a measured hemorrhage was being inflicted?

Answer: Within tolerable limits, this appears to be the case. In 7 dogs undergoing a continuous hemorrhage calculated to remove 35% of their blood volume in four hundred minutes, the plasma volumes were compared at one hundred minutes using T-1824. The mean of the differences was 34.8 ± 24.4 ml. (4.9 ± 4.5%). In 6 of these dogs, using a second RIHSA injection at two hundred minutes, the mean of differences was 2.3 ± 34.7 ml. (0.7 ± 6.8%). These data strongly vindicate a method which has multiple advantages (a single injection, no accumulation of base line intensity, and an almost limitless number of observations), provided that the limited conditions in which it is valid prevail.

In summary of this section, therefore, we may say that a technique has been devised which can measure continuously plasma volume for at least a three-hour period with acceptable accuracy under certain fixed circumstances, including the experimental and control animals in this series of studies. A mean disappearance curve for a single dose of RIHSA in splenectomized dogs under light pentobarbital anesthesia in Denver, Colorado, has been constructed which predicts with

TABLE 3

COMPARISON OF PLASMA VOLUMES DETERMINED BY A SINGLE RIHSA INJECTION AS CALCULATED FROM A TEN-MINUTE SAMPLE AND FROM EXTRAPOLATION

Mean volume (ten minutes)	953. ml.
Mean volume (extrapolation)	946. ml.
Mean difference	+6.5 ml. (+0.6%)

TABLE 4

MORTALITY WITH VARIOUS VOLUMES OF ACUTE ARTERIAL HEMORRHAGE

Hemorrhage (percent of blood volume)	*Number of dogs*	*Mortality rate (percent)*
35	34	0
39	4	25
42	11	45
45	9	89

remarkable accuracy what the concentration of I^{131} in the plasma would be at any moment for three hours after injection. Any change in the expected blood volume, therefore, that is brought about by the experimental procedure can be quantitated.

Predictability of mortality due to hemorrhage. The relationship between various volumes of bleeding and mortality rate in this preparation proved to be remarkable, provided, as will be discussed below, the experiments are done within a short span of the solar year. For example, a series of experiments performed in the spring months resulted in the data presented in table 4. These data are presented graphically in figure 4 for emphasis.

If this same data were subjected to mathematical analysis and plotted as the percent mortality against the logarithm of the percent of the blood volume removed, the remarkable straight-line relationship illustrated in figure 5 is seen. We concluded, therefore, that in the lightly anesthetized, stable, splenectomized dog a remarkably consistent mortality rate is associated with any specific rapid arterial hemorrhage when the selected bleeding volume is a fraction of the measured blood volume of the animal. This consistency was of such a degree that it allowed high predictability. Figure 6 presents a probit analysis with 95% confidence limits depicted in broken lines. From this analysis, it would be possible to predict, for example, that the $L.D._{50}$ bleeding volume will be 42 or 43% of the total blood volume and that there are 19 chances in 20 that 50% of a group of animals (10 or more) bled in this fashion will die. Clearly, the experimental model gave great promise as a research tool.

We thought it interesting that the band separating zero mortality from 100% mortality was so narrow, that is, only about 10% of the blood volume. If an animal were bled 35%, no mortality was seen, but if 45% were lost, only a rare animal will survive. One might conclude that, clinically, the margin of safety in acute hemorrhage is small and that in the support of blood volume a

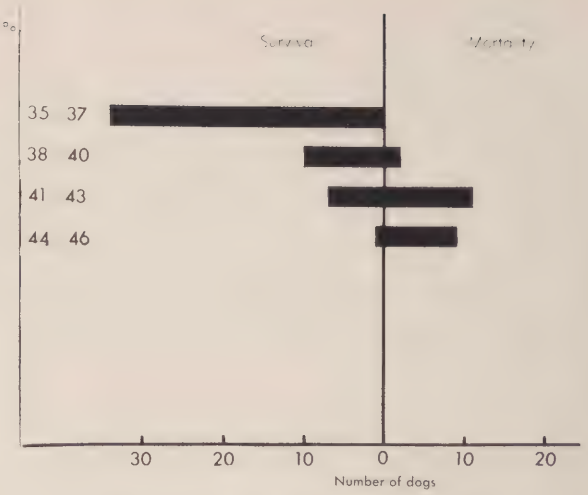


Fig. 4. Percentage of blood volume hemorrhage

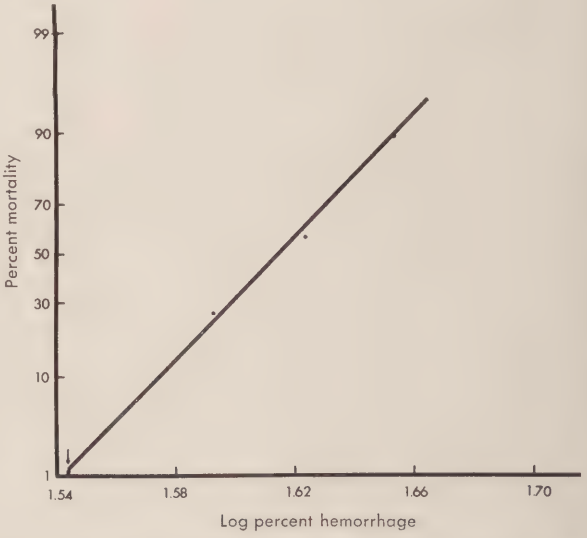


Fig. 5. Mortality of anesthetized dogs due to hemorrhage

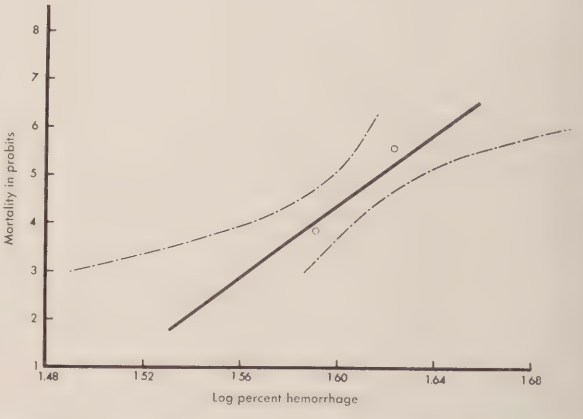


Fig. 6. Mortality from hemorrhage with 95% confidence limits

TABLE 5

ACUTE HEMORRHAGE: PERCENT MORTALITY OF VARIOUS BLEEDING VOLUMES BY MONTHS

	Oct. to Nov.	*Dec. to Feb.*	*Mar. to May*	*July to Aug.*
34.2%	0	—	0	25
36.7%	12.5	—	0	37.5
39 %	12.5	—	12.5	100
41.5%	62.5	50	—	—
44.2%	—	50	87.5	—

few hundred milliliters of blood given early may well be more important than full replacement given after irreversible changes due to hypovolemia have occurred. In man, control of the hemorrhage and 1 bottle of dextran given by an ambulance attendant at the scene of an accident are probably much better than screaming sirens and 6 units of blood given an hour later in the hospital.

The effect of season on the response to hemorrhage. Early in our attempts to use the predictability of hemorrhage volume and mortality we ran into serious difficulties. After much painful reassessment of techniques, data, and analyses, we began to realize that the preconditioning of the animal was an important variable and that the season of the year when the experiment was performed was a critical parameter. Our animals following splenectomy were kept in cages and then runs that were open to the air and were, therefore, subject to seasonal variations in temperature. A series of bleedings was done in which similar volumes were withdrawn at intervals throughout the year. Very significant differences in mortality rate were soon apparent. The data from this experiment are shown in table 5. It is clear that during the summer months a hemorrhage of a given volume is much more serious than a similar hemorrhage in winter. This recalls to mind the fact that Larry, Napoleon's chief surgeon, commented on the better ability of soldiers from Northern France to survive the wounds of battle than those from the Midi. Perhaps the historical fact that a Norman can usually conquer a Neopolitan has a scientific basis in the physiology of preconditioning.

An extremely important corollary of these observations relates to all work on experimental hemorrhage and, probably, also to shock of all types; namely, it is imperative that all studies be done with paired controls and procedures that are performed at the same time. Experimental hemorrhage in December cannot be compared with that of controls performed in August. Certainly much confusion and conflicting data in the studies published by different investigators may be related to this phenomenon.

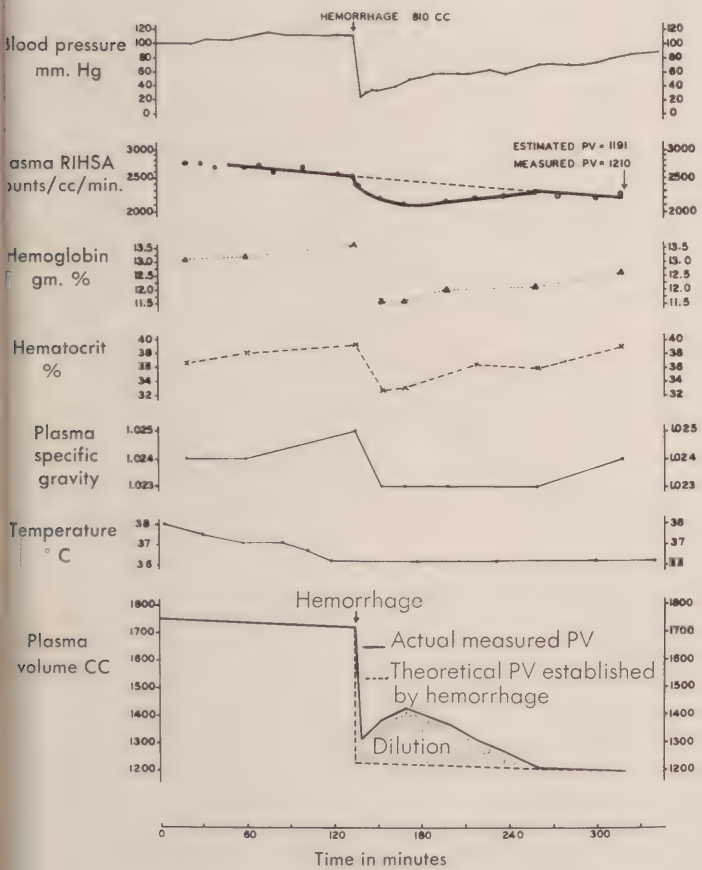


Fig. 7. Hemorrhage of 35% of volume in normothermic dog weighing 23.2 kg. (Ann. Surg. 144:696, 1956. Wilson, Marshall, Beresford, Montgomery, Jenkins, and Swan)

EXPERIMENTAL DATA

Blood volume changes in acute hemorrhage. A suitable animal to study for changes in blood volume is one which is bled of 35% of its initial blood volume. The animal almost invariably survives, but the insult results in a rapid fall in blood pressure, followed by shifts in fluid volumes. Figure 7 graphs the data obtained in a typical experiment. All the parameters measured were quite stable before the hemorrhage was inflicted. Blood pressure fell abruptly and an extremely rapid transfer of fluid into the plasma occurred, as demonstrated by the concentration changes. The hematocrit of the last 10 ml. of the blood withdrawn was lower than that of the first 10 ml., even though the bleeding was accomplished in about four minutes. Fluid had begun to enter the plasma in measurable amounts in this time interval. Thus, before hemorrhage had been concluded but after a significant fall in blood pressure had occurred, the blood was al-

ready dilute. Water continued to enter the plasma in this animal until it reached a peak at about one-half hour after the bleeding, as noted in the bottom lines of the graph, which illustrate both the actual (line above stippled area) and the virtual plasma volume (that is, the plasma volume that would have remained after a 35% hemorrhage if no fluid shift occurred). The height of the stippled area at any one minute represents the actual volume of fluid which has entered and at that moment remains in the vascular compartment. It is expressed in terms of the percentage of the original plasma volume. Thus, at one-half hour in this animal, although 35% of his original plasma volume had been removed with his bleeding, fluid in an amount equivalent to 17% of his original plasma volume has now entered the bloodstream.

The interesting observation in these experiments was the course of events in the next hour and a half. The fluid which had entered the plasma leaked back out again so that at the end of the three-hour experiment the blood volume was again 35% deficient.

Meanwhile, the blood pressure, which had fallen so abruptly, immediately started a slow and steady recovery and reached normal levels by the conclusion of the experiment. This response seems to be due to factors other than the plasma dilution because, as the blood pressure is rising, the fluid is actually leaving the plasma. A possible relationship between these 2 phenomena is discussed below.

In any event, at the three-hour mark in this experiment, the blood pressure is normal, the hematocrit is normal, and yet the measured blood volume is only 35% of normal. Clearly, other changes must occur with further time, but at this moment 2 important clinical measurements were normal in an animal with dangerously low blood volume. The sudden loss of only a few additional milliliters of blood might well have been lethal.

We belive this observation has important clinical implications. One is that the blood pressure determination may be a treacherous indicator of the state of the circulation under certain conditions. Another is that the hematocrit determination alone cannot be relied upon to reflect accurately changes in blood volume. (At the three-hour moment the hematocrit was normal.) Such an interpretation must include a measured plasma volume!

Hypothermia and hemorrhage. It had been suggested that cooling might be desirable in the treatment of the injured patient. Some evidence had been presented that prolonged hypotension

TABLE 6

MORTALITY RATE OF DOGS BLED OF 35% OF BLOOD VOLUME AT DIFFERENT TEMPERATURES

Temp. range	*Number*	*Died*	*Percent mortality*
40° to 35°	24	0	0
31° to 28°	13	1	8%
26° to 20°	22	18	82%

was better tolerated in the cooled dog. Therefore, we tested the effect of bleeding a similar volume of blood from dogs who had been cooled to different body temperatures. Table 6 presents these results. The bleeding volume chosen was 35%, which in the normothermic animal resulted in zero mortality. At moderate hypothermia (31 to 28° C.) 1 animal of 13 died, but at the lower range of 26 to 20° C. the mortality was 82%.

It was interesting that as the animals were cooled there was a progressive inability of the animals' responses to restore blood pressure after the hemorrhage. Figure 8 presents 4 families of blood pressure curves at different temperature levels. One notes that the absolute fall in pressure was less in the colder groups, largely because it started from a lower (hypothermic) level. In addition, however, it did not respond as well, and in the coldest group almost all the animals died. This figure will be referred to again in the discussion on the possible relationship between pressure changes and fluid shifts. However, we believe that the explanation for the inability to restore blood pressure in these animals is primarily due to paralysis of their vascular reflexes due to cold. We learned from other

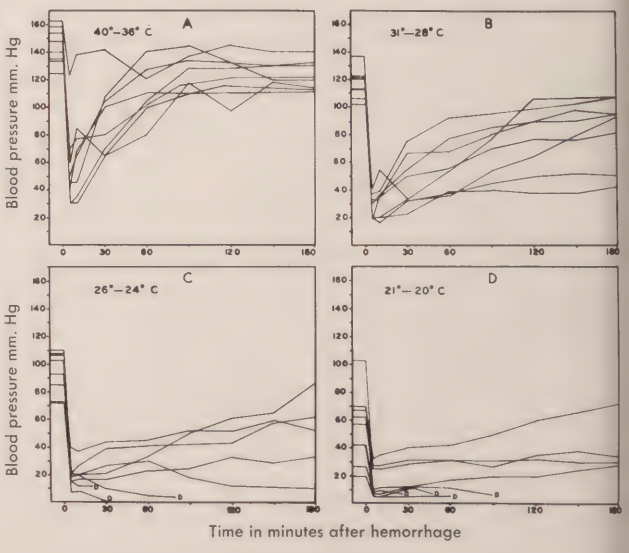


Fig. 8. Blood pressure response following hemorrhage at different temperatures (Ann. Surg. 144:696, 1956)

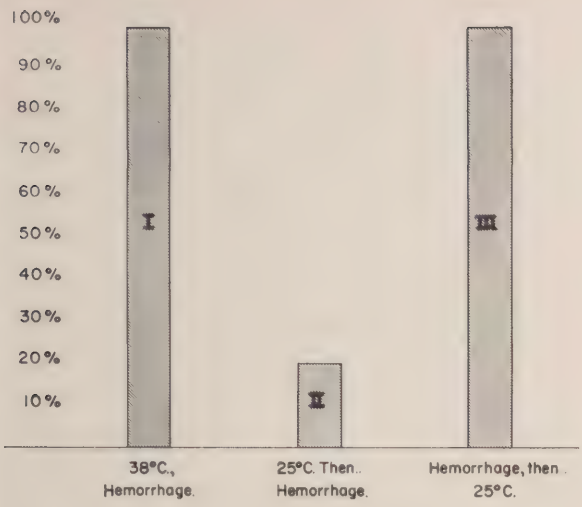


Fig. 9. Survival following rapid hemorrhage (35% of blood volume) (Ann. Surg. 147:281, 1958. Ferguson, Wilson, Jenkins, and Swan)

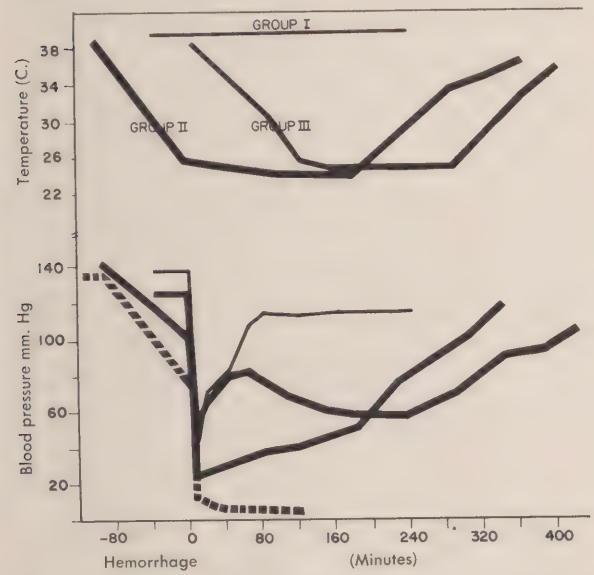


Fig. 10. Relationship of mean temperature to mean blood pressure following hemorrhage

studies in man that many basic reflexes are lost at about 28° C., due to the nerve blocking effect of cold. In any event, it was clear that as an animal was progressively cooled he tolerated a standard hemorrhage less and less well.

The clinical lesson from these experiments corroborated our experience at the operating table. When hypothermia is used for various operative purposes, such as severe sepsis, hyperthyroidism, cerebral aneurysm, portacaval shunt, or cardiac surgery, blood replacement must be quite adequate and right on time, since the margin of safety from hemorrhage is sharply curtailed.

This experiment did not answer the question, however, of whether cooling an animal after the bleeding would be beneficial. We attempted to answer this, but we think that probably a more lethal initial hemorrhage in our experimental design would have been more conclusive. Three groups of animals were bled of 35% of their blood volume; the controls were at normal temperature, a group at 25° C. rectal temperature, and finally a group at normothermia and then immediately cooled to 25° C. Figure 9 presents in bar-graph form the results of this experiment. Since none of the controls died, it is hard to conclude whether subsequent cooling was beneficial or not. At least at this level of hemorrhage it did not add to the mortality rate. In the 25° C. dogs a high mortality was seen, corroborating our earlier experience that cold dogs do not tolerate hemorrhage, and the blood pressure response, namely, a slower return in the precooled animals and a delayed response in the postcooled animals, was observed as expected. These data are graphed in figure 10. The question of the place, if any, of deliberate hypothermia in the treatment of hemorrhage needs further elucidation.

Blood pressure changes and fluid shifts. As this work progressed over the years, it seemed more and more as if there might exist a causal relationship between blood pressure changes and fluid shifts into the plasma and that this relationship might be the exact opposite of what has long been a common conception. We think it is fair to state that most physicians have believed that following hemorrhage or acute hypovolemia of any cause the plasma is augmented by the entrance of fluid and electrolytes into the bloodstream and that this increment in blood volume was a compensatory mechanism largely responsible for maintenance of normal or recovery from lowered blood pressure. The evidence in this series of experiments, however, strongly suggests that following acute arterial hemorrhage the recovery of the blood pressure is primarily due to vascular readjustments of a reflex nature, that it is not significantly influenced, within nonlethal limits, by early fluid augmentation of plasma volume, and, indeed, that the volume of the fluid shifts may be determined by the blood pressure changes. The evidence we have for this concept may be summarized as follows.

Attention is redirected to the sequence of events following a 35% hemorrhage in the normothermic dog, with interest focused on the blood pressure changes and the fluid shifts during the first two and a half hours following the hemorrhage. These 2 parameters from the data given

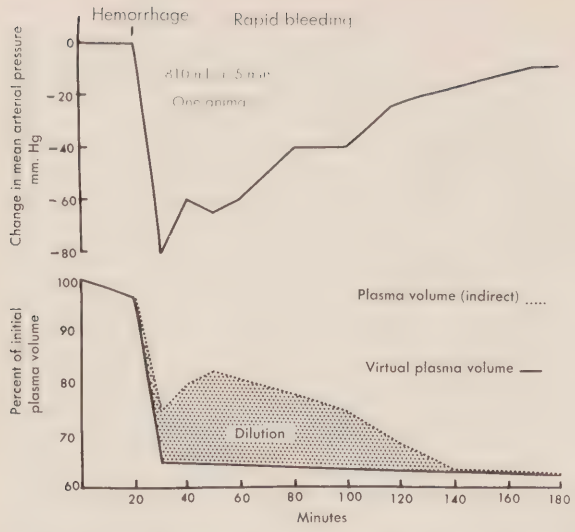


Fig. 11. Blood pressure changes and fluid shifts during first two and a half hours after hemorrhage (Arch. Surg. 82:72, 1961. Jenkins, Hataya, Marchioro, Montgomery, and Swan)

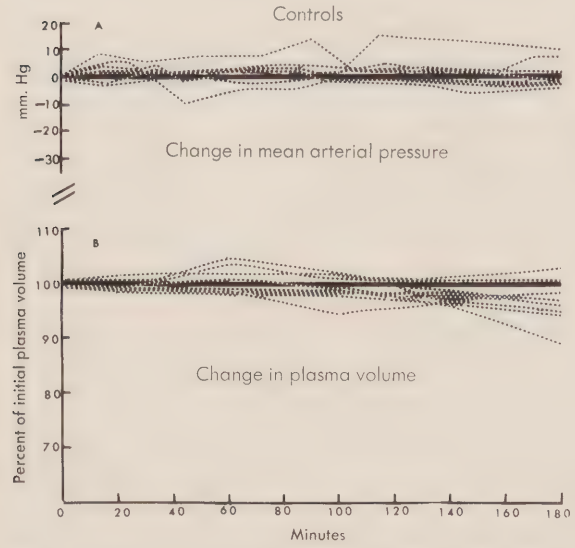


Fig. 12. Blood pressure and plasma volume after hemorrhage of 2% of initial blood volume over three-hour period (Arch. Surg. 82:69, 1961)

in figure 7 are presented together again in figure 11. To reemphasize the method of graphing, the bottom solid line in the lower diagram is the so-called virtual plasma volume. It represents the computed volume which would be present after 35% of the original volume has been withdrawn, if no fluid shifts occur. It is a theoretical volume, but on occasion, as in this instance, it may become the actual volume. The thinner line above the stippled area indicates the actual measured plasma volume using our method of the mean disappearance curve.

Inspection of this figure reemphasizes that the fall in blood pressure was very abrupt with the rapid hemorrhage, that dilution of the plasma had occurred before the hemorrhage was completed, that the dilution reached its peak one-half hour after the hemorrhage and then all the water of augmentation returned to other spaces as the plasma volume shrank until actual and virtual volumes were the same, and that blood pressure rose steadily, especially during the period when the plasma was losing its water of augmentation. In this graph, when blood pressure falls, water enters the plasma; when pressure rises toward normal, fluid leaves the vascular compartment and plasma volume falls.

A series of experiments was now performed under one of the most prolonged, rigid, and exacting protocols ever performed in our laboratory. We attempted to compare fluid volume shifts in response to similar-size bleedings, one done rapidly and the other done slowly over a period of time. Again, the withdrawal of 35% of initial blood volume was selected for the "slow bleeding" experiment because its effect on blood pressure and fluid shift when done rapidly was so well known in our laboratory. The hemorrhage was performed by 18 equal withdrawals done at ten-minute intervals. Thus, after a period of preparation, anesthesia, insertion of cannulas, and stabilization which usually lasted one and a half or two hours, a three-hour experiment was not conducted which required the continuous, active, careful, repetitive participation of the research fellow. Dr. Hataya's quota of oriental aplomb may have played a major role

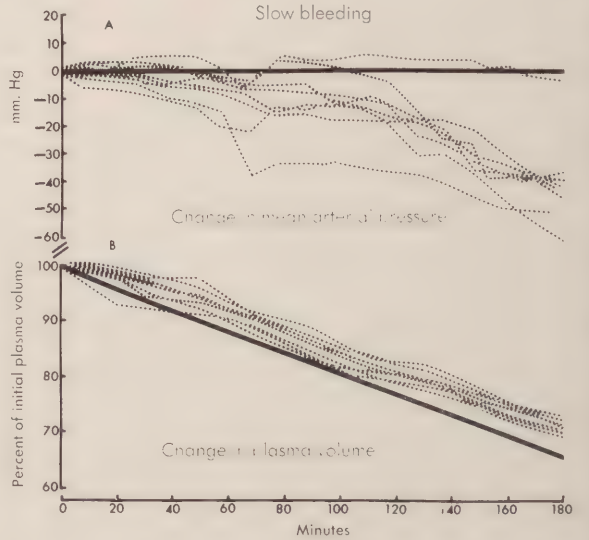


Fig. 13. Mean blood pressure and plasma volume of 8 dogs with slow bleeding (Arch. Surg. 82:69, 1961)

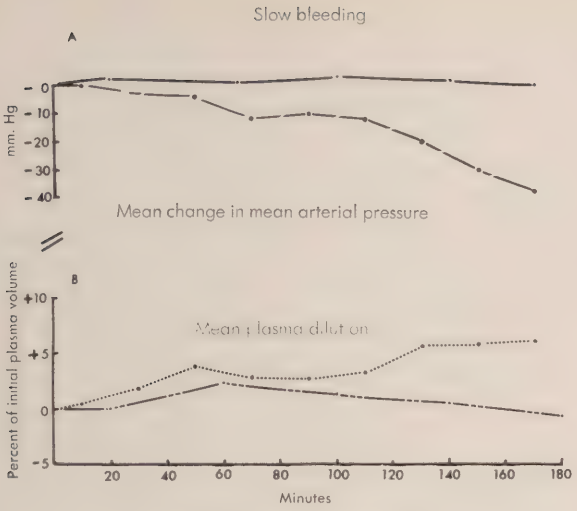


Fig. 14. Graph of figure 13

in the successful outcome of this experiment as he imperturbably repeated this sequence every ten minutes. He checked the pupillary reflexes (if needed, additional pentobarbital was given); he observed the mean blood pressure and recorded it; he withdrew 2 ml. of blood into a syringe, discarding the blood to clear the tubing; he then withdrew into a syringe the indicated bleeding volume, putting half into each of 2 test tubes for laboratory analysis of hematocrit and plasma volume; and finally he reinserted 2 ml. of heparinized blood into the tubing to avoid clotting. He then recorded the volume and time of the bleeding in the protocol book. This carefully timed sequence was repeated ceaselessly for three hours, when the experiment was concluded.

A group of 9 animals served as controls for this experiment. In these dogs after insertion of cannulas and after stabilization from anesthesia, blood was drawn for sampling only every ten minutes for three hours. Only 2% of the initial blood volume was withdrawn in all. Both blood pressure and plasma volume remained quite stable during the period, as illustrated in figure 12.

In the experimental group of 8 animals, the data on mean blood pressure and plasma volume are presented in figure 13. These raw data for both groups were analyzed and the means of both groups graphed in figure 14. In the controls, there was a slight rise in plasma volume for one hour and then a gradual decline to normal (bot-

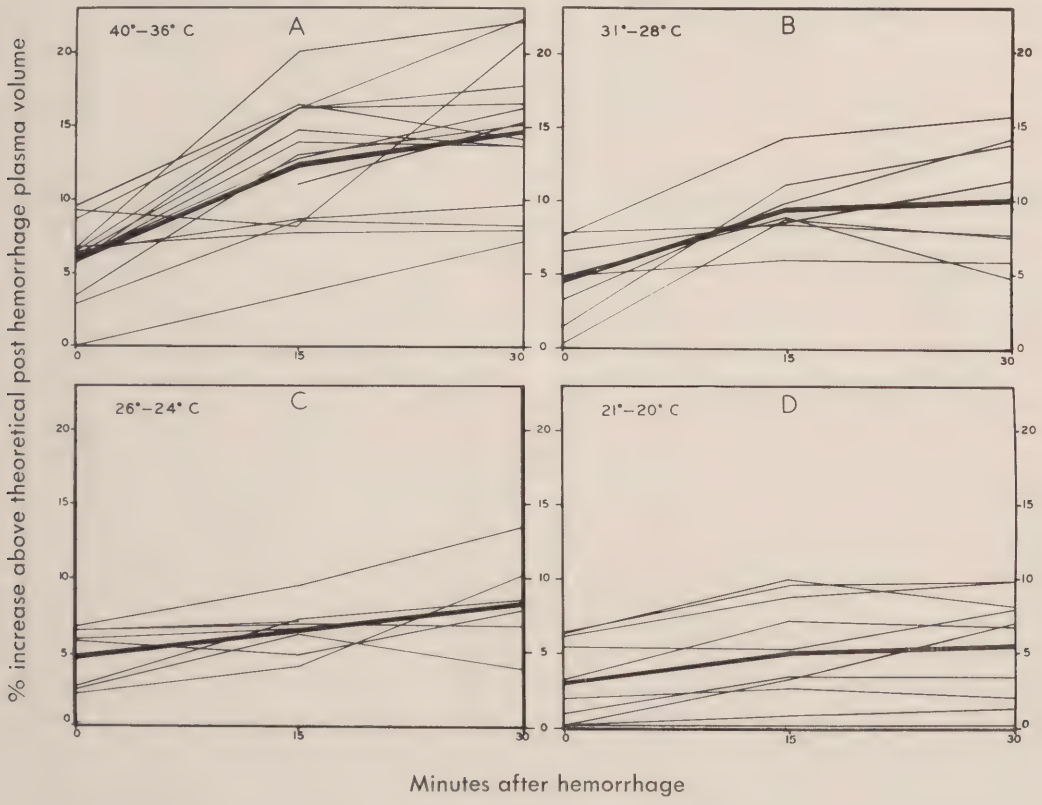


Fig. 15. Effect of temperature on plasma dilution following hemorrhage (Ann. Surg. 144:696, 1956)

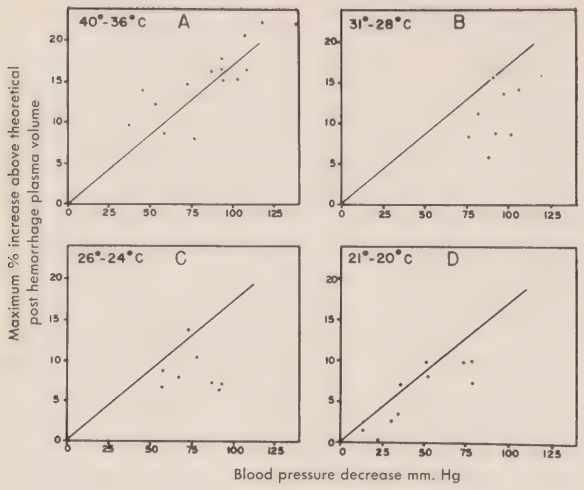


Fig. 16. Correlation between maximum plasma dilution and blood pressure decrease by temperature groups (Ann. Surg. 144:696, 1956)

tom line of 14B). The blood pressure remained level (top line of 14A). In contrast, in the animals with slow hemorrhage, the mean arterial pressure fell very slightly after one hour and then stabilized for almost another hour. The pressure then fell more precipitously as the last third of the bleeding volume was removed. As seen in the upper line in 14B, the plasma dilution paralleled almost exactly the blood pressure fall in time, and the quantitative alterations in each parameter were comparable.

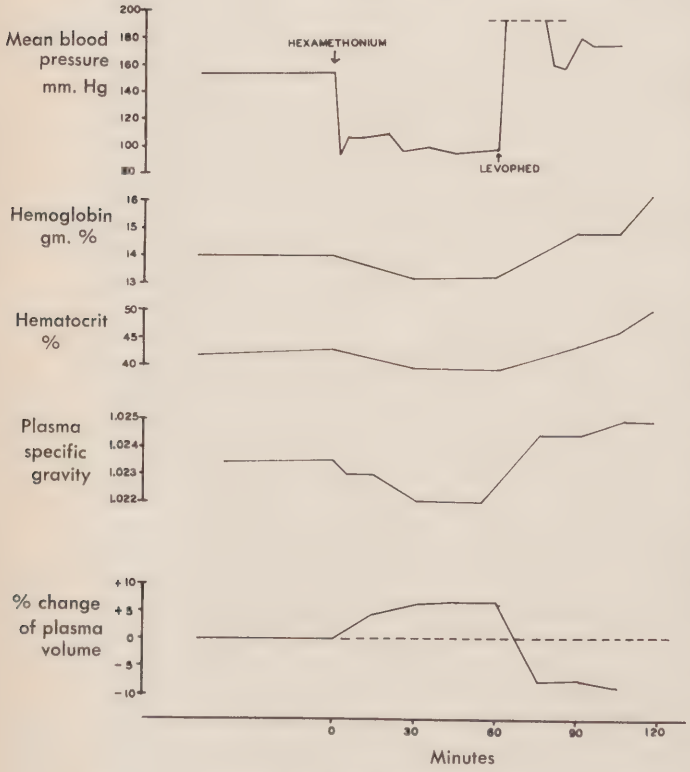


Fig. 17. Response of unanesthetized dog to hexamethonium and Levophed®

It will be recalled that in the experiment studying the effect of hypothermia on mortality following hemorrhage the mean arterial pressure curves showed a smaller and smaller fall in blood pressure as the level of hypothermia was deepened (Fig. 8). There was, under these conditions, a parallel decrease in the amount of plasma dilution which occurred. These data are graphed in figure 15; the means are plotted as the heavy line for each temperature group. Once again, when blood pressure falls were less, plasma dilution was less. The correlations in this experiment were best at normal temperature and at the coldest temperatures (21 to 20° C.), as can be seen when the data are charted as maximum percentage increase in plasma volume against the blood pressure decrease in millimeters of mercury (Fig. 16).

If profound blood pressure changes influence fluid shifts, one might expect significant changes in plasma volume as a result of drug-induced hypotension. An early experiment with a quiet but unanesthetized dog of the effect of hexamethonium chloride is illustrated in figure 17. After the injection of a standard dose, the blood pressure fell to 50 mm. Hg. Fluid immediately entered the plasma which became dilute. The volume of the shift was equal to about 9% of the original plasma volume. The blood pressure stayed at a depressed level and the plasma remained dilute for one hour. Norepinephrine (Levophed®) was then administered. The blood pressure shot up immediately to hypertensive levels, and the plasma lost its dilution at once; in fact, it became smaller than its original volume by about 12%. In this experiment, then, lowering and raising blood pressure by pharmacological means was followed immediately by significant changes in plasma volume.

Recently, a small series of 4 animals receiving trimethaphan camphorsulfonate (Arfonad®) was studied. The mean changes in blood pressure and the mean plasma dilution after the injection of 20 mg. per kilogram intravenously are presented in figure 18. The virtual plasma volume slopes gradually because an average of 70 ml. of blood was removed for the sampling. Thus, about 5% of the blood plasma was removed in equal increments during the experiment. Once again, one sees the early augmentation of the plasma with escape of the fluid concomitant with the return of blood pressure toward normal.

Finally, when all the data from the experiment

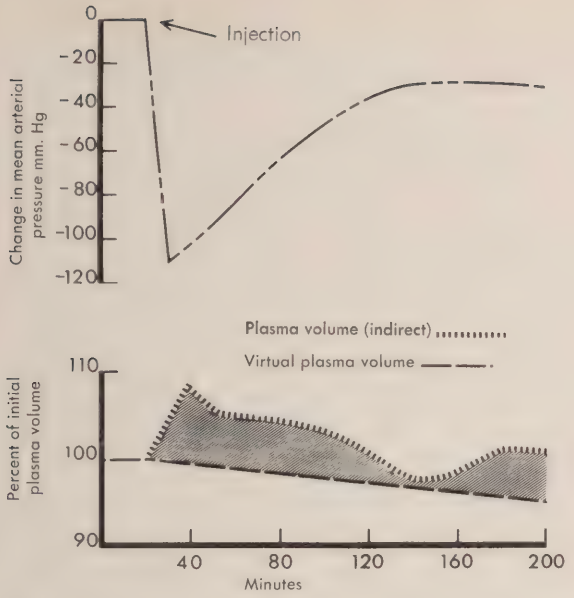


Fig. 18. Mean changes in blood pressure and plasma dilution after injection of Arfonad®

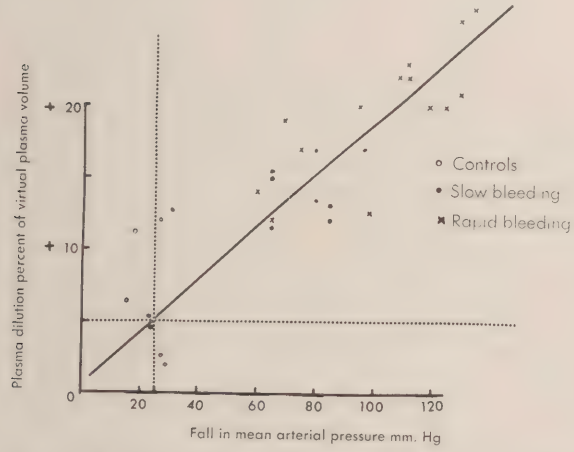


Fig. 19. Relationship between change in arterial pressure and plasma dilution (Arch. Surg. 82:69, 1961)

of slow bleeding plus those from 15 animals previously reported who were bled of 35% of their blood volume in five minutes were charted as plasma dilution in percentage of virtual plasma volume against fall in mean arterial blood pressure in millimeters of mercury, the graph in figure 19 emerged. It is clear that under the conditions of these experiments there is excellent correlation between the magnitude of blood pressure fall and the magnitude of the plasma dilution.

DISCUSSION

In accordance with the Starling hypothesis, the pressure gradient betwen the arterial and venous end of the capillary loop crosses the mean osmotic pressure of plasma; therefore, fluid tends to leave the arterial capillary and to reenter the venous capillary. If a lowering blood pressure does, in fact, lower the arterial capillary pressure then the factors favoring the entrance of fluid into the bloodstream would overbalance those favoring its exit, and fluid would accumulate in the intravascular space. As it does so, however, the plasma becomes dilute and the osmotic pressure must decrease. This factor, working in the opposite direction, might finally cause an equilibrium in fluid exchange at a level lower than before the pressure drop. We have never seen the fluid of plasma augmentation exceed 50% of that which was removed with hemorrhage; usually it is less.

Since the water and salt absorbed across the capillary from the surrounding tissue spaces is relatively protein-poor and, hence, osmotically weak and if the forces tending to extrude fluid from the bloodstream improve, that is, a rise in arterial capillary pressure with rising blood pressure, the weakly osmotic plasma readily loses water and salt again to the extracellular tissue spaces. This may be the explanation of our rather constant finding in experimental hemorrhage of 35% of the blood volume that the measured plasma volume at the end of three hours (although for a time it had been augmented) had returned to virtual volume, that is, was 35% deficient. Later, at twenty-four hours, the plasma volume had increased and the blood was dilute, as documented by a low hematocrit. Gradually, fluid had entered the vascular compartment and had remained there, even though the blood pressure remained normal. We suggest that this is further evidence that a slower homeostatic mechanism comes into play, possibly the entrance of protein-rich fluid into the bloodstream via the thoracic duct. This plasma dilutant is osmotically potent and therefore remains in the vascular compartment in the presence of normal capillary pressure gradients. Thus, plasma volume and, hence, blood volume gradually improve.

We believe that the experiments also suggest that the return of blood pressure following hemorrhage is more likely a result of widespread cardiovascular reflexes and the shrinking of large vessels, probably venous, reducing the size of the vascular bed. Augmentation of the plasma by fluid shift does not appear to be the prime cause of the pressure recovery, as this fluid is promptly lost as the pressure rises.

A prime clinical lesson to be derived from

these experiments, we suggest, is a healthy suspicion of commonly used observations in the evaluation of certain patients. After acute arterial hemorrhage or major surgery, a patient may have a normal blood pressure and a normal hematocrit and, yet, his blood volume may be precariously low. Unless adequate blood replacement has in fact been performed, this patient is in a critical state which appears deceptively benign. Actual blood volume determinations and central venous pressure measurements would be necessary to elucidate the situation.

We propose next to direct our attention in the experimental laboratory to the occurrences in the time interval between three and twenty-four hours after hemorrhage and to study the volume and composition of thoracic duct lymph, as well as changes in the blood plasma.

These studies were supported by a contract with the Surgeon General, U.S. Army (VC3HS64), and by a grant from the U.S. Public Health Service, No. H2710.

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SERIAL OXIMETRY may fail to detect small left-to-right shunts while a patient with septal defect is breathing air. Detection is improved if 100% oxygen is administered during oximetry to exaggerate the step-ups in oxygen saturation which are diagnostic of the shunts. Serial oximetry during oxygen administration led to left-to-right shunt diagnosis in all of 8 patients with septal defect, whereas shunts were detected in only 4 during air-breathing.

JAMES N. KARNEGIS, M.D., and YANG WANG, M.D., University of Minnesota, Minneapolis. Amer. J. Cardiol. 13:64-70, 1964.

MULTIPLE BIOPSY specimens along the gastrointestinal tract—from stomach to ileum—can be obtained with a simplified suction biopsy capsule made up of 2 concentric stainless steel shells that resemble halves of a standard gelatin capsule. When the capsule is open, holes in each half are superimposed. A fine plastic catheter is attached to the upper half. A rubber bag containing mercury attached to the lower half eases passage of the capsule through the pylorus and along the small bowel. The device reaches the 100-cm. level in one to five or more hours. When the capsule is at the desired level, saline solution or water is injected through the plastic catheter with a 100-ml. syringe to flush intestinal contents from tube and capsule. The plunger is pulled back to the 100-ml. mark to apply suction for a few seconds to pull mucosa into the capsule; continued suction closes the capsule, shearing off a piece of mucosa. The capsule is spring-loaded, so by releasing suction, withdrawing the tube a few centimeters, and then reapplying suction, further specimens are obtained.

JAMES B. CAREY, JR., M.D., University of Minnesota, Minneapolis. A simplified gastrointestinal biopsy capsule. Gastroenterology 46:550-557, 1964.

Renal Insufficiency and Pancytopenia in Subacute Bacterial Endocarditis

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In the preface to *Clinical Heart Disease*, Dr. Samuel Levine[1] stressed the importance of expending our prime efforts in searching for potentially treatable or correctable diseases. Since both azotemia and pancytopenia often accompany illnesses that have, at best, a poor prognosis, we wish to report the following case of subacute bacterial endocarditis, complicated by both renal insufficiency and pancytopenia.

CASE REPORT

A 35-year-old female was admitted to Hollywood Memorial Hospital because of hematuria and fatigue. For several weeks before admission, the patient had noticed increasing fatigue, nausea, anorexia, and modest edema of both ankles. There was also increasing pallor. The patient had always enjoyed good health and specifically denied knowledge of rheumatic fever, scarlet fever, or renal disease. At ages 14 and 26, the patient was informed during routine physical examinations of the presence of a heart murmur that was considered to be of little importance.

There was no recent dental work and no recent drug ingestion. Two weeks before admission, however, while working as a meat packer, the patient accidently had a sliver of bone thrust into her finger. A small infection ensued, but no medical advice was obtained and the lesion cleared spontaneously.

On the day of admission the patient had considerable discomfort in the lower abdomen associated with gross hematuria. The hematuria was confirmed by microscopic examination of the urine.

Physical examination disclosed a blood pressure of 126/84. The apical pulse was 110 and regular, with an oral temperature of 101.8° F. There was marked pallor. The neck veins were flat and there was no enlargement of the thyroid gland. The lung fields were clear. The heart was enlarged with a forceful diffuse point of maximum impulse felt and visualized 2 cm. lateral to the midclavicular line in the sixth intercostal space. There were no thrills. There was a grade 4/6, blowing, pansystolic, apical murmur with radiation to the axilla. There was also a grade 2/6, low-pitched, presystolic rumble leading to a loud M-1. P-2 was accentuated, but an opening snap was not heard.

The spleen was palpable 4 cm. below the left costal margin; hepatomegaly was not evident. Examination of the extremities and neurological evaluation were unremarkable.

Laboratory examination showed hemoglobin 5.8 gm. percent; hematocrit 18%. White blood count was 2,700 per cubic millimeter with 68% polymorphonuclear leukocytes, 5% band forms, and 27% lymphocytes. The platelet count was 96,000 per cubic millimeter. Urinalysis revealed 2 plus albumin and many red blood cells. The blood urea nitrogen was 70 mg. per 100 ml. Other pertinent laboratory findings were 3 negative lupus erythematosus cell preparations, normal electrolytes, and a 23% bromsulphalein retention in forty-five minutes. There was a positive direct Coombs test. The serum glutamic oxalacetic transaminase was 21 units, and the antistreptolysin titer was 150 Todd units.

Three blood cultures drawn on the day of admission grew out a highly sensitive alpha streptococcus.

The patient appeared to be extremely toxic with spiking temperatures to 102° F. for the first seventy-two hours of hospitalization. A bone marrow aspiration showed a moderate increase in mature plasma cells with an active marrow. There was no evidence of any specific hematological entity.

With fever, splenomegaly, hematuria, and evidence of rheumatic heart disease with both mitral stenosis and insufficiency, a clinical diagnosis of subacute bacterial endocarditis was made and the patient was begun on 2,400,000 units of penicillin intramusculary and 2,400,000 units by slow intravenous drip daily. In addition, probenecid,

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0.5 gm. twice daily, and oxytetracycline, 500 mg. every six hours, were also administered. In view of the pancytopenia, steroid therapy was also initiated.

When the blood cultures showed a growth of a highly sensitive alpha streptococcus, the oxytetracycline was discontinued.

Within seventy-two hours after initiation of therapy, the patient showed remarkable clinical improvement. With transfusions and steroids, the hemoglobin was maintained at approximately 12.5 gm. percent, and the white blood count rose to 10,000 per cubic millimeter. The platelet count also increased 250,000 per cubic millimeter. Repeat blood cultures were negative.

However, in spite of the clinical improvement and the abatement of the fever, the patient continued to have microscopic hematuria, albuminuria, and severe azotemia, with the blood urea nitrogen reaching a peak of 156 mg. percent on the ninth hospital day. Urinary output was adequate throughout hospitalization, averaging between 1,400 and 2,000 cc. daily.

After the ninth day, however, the blood urea nitrogen began to fall slowly to a low on the day of death of 108 mg. percent. The clinical improvement continued until the sixteenth hospital day when the patient suddenly experienced a severe occipital headache followed by rapidly progressive coma and death.

POSTMORTEM

Pertinent autopsy findings were as follows:

The heart weighed 330 gm. with left ventricular hypertrophy. There was 100 cc. of straw-colored pericardial fluid. There was an old mitral valvulitis with rolled thickened leaflets and short chordae tendineae. There were fresh vegetations on both anterior and posterior mitral leaflets.

Microscopically, there was evidence of both old healed rheumatic valulitis and subacute bacterial endocarditis. Organisms, however, were not visualized. The lungs showed marked congestion and edema, both grossly and microscopically.

Examination of the gastrointestinal tract revealed congestive hepatomegaly (2020 gm.) and septic thrombi in a small splenic vessel with secondary infarcts, the largest of which measured $3 \times 3 \times 2.5$ cm. The spleen weighed 220 gm. In addition, there was a septic thrombus in the superior mesenteric artery and in the mesenteric radicals with small mycotic aneurysms.

The kidneys together weighed 660 gm. They were large, soft, and the cortices were dotted with petechial hemorrhages. There were also petechial hemorrhages in the renal pelvis and calyces. Microscopically, there was both a diffuse subacute glomerulonephritis and focal embolic glomerulonephritis (Fig. 1). The tubules contained fresh blood and there were small scattered foci of acute pyelonephritis.

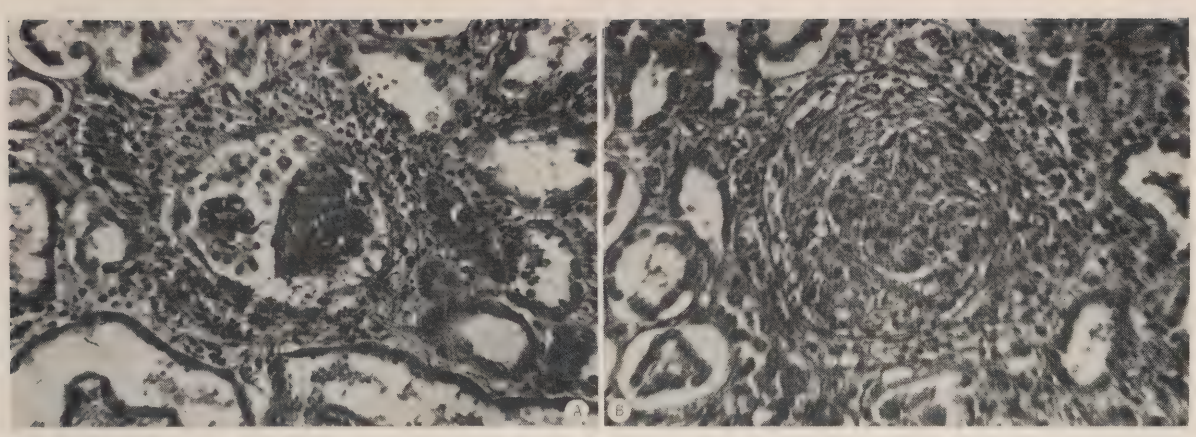
The immediate cause of death was a massive intracranial hemorrhage arising in the left parietal occipital area with rupture into the left ventricle with subsequent subarachnoid hemorrhage. There was a cerebellar pressure cone. In spite of careful dissection, the vessel responsible for the hemorrhage could not be found.

DISCUSSION

Renal involvement is common in subacute bacterial endocarditis. In a recent review[2] of 167 patients with bacterial endocarditis, 63% were noted to have pyuria, 49% proteinuria, and 46% microscopic hematuria. Elevations in blood urea nitrogen were observed in 44% of the patients studied. In a recent monograph on subacute bacterial endocarditis[3] abnormalities in urine sediment were present in 50 to 95% of the patients studied.

The presence, however, of significant azotemia and renal insufficiency is less common. In a study of 100 patients dying of subacute bacterial endocarditis,[4] there were 14 patients with severe renal insufficiency with 9 additional patients showing less marked evidence of renal failure. In a cooperative study of 442 patients with subacute bacterial endocarditis from 14 medical centers in Great Britain,[5] there were 18 patients dying in renal failure. Ten of the 18 patients also had congestive heart failure. It was somewhat discouraging to note that 16 of the 18 deaths due to renal insufficiency occurred in patients in whom the infection was apparently controlled with penicillin.

Focal embolic glomerulonephritis is the best known of the renal lesions in subacute bacterial endocarditis. However, it is not often appreciated that a diffuse, acute, glomerulonephritis may also complicate subacute bacterial endocarditis. The reason for this lack of awareness may be the result of the apparent confusion and inconsistency in the literature over the exact frequency of this more diffuse glomerulitis. In the latest edition of Harrison's *Principles of Internal Medicine*,[6] it is stated that a "diffuse glomerulitis is commonly encountered." However, in a series of 52 cases recently reported,[7] only 1 patient had microscopic evidence of a diffuse glomerulitis. In a case reported by Flood and Boller,[8] diffuse proliferative glomerulonephritis was described as "an unusual complication of subacute bacterial endocarditis."



(A) Focal embolic glomerulonephritis. Hematoxylin and eosin, × 320. (B) Diffuse proliferative subacute glomerulonephritis. Hematoxylin and eosin, × 320.

Earlier studies,[9,10] however, reported a diffuse glomerulonephritis as occurring in 65 to 80% of kidneys examined in fatal cases of subacute bacterial endocarditis. A more recent study[4] which showed the diffuse glomerulitis to be as common as the embolic would appear to lend support to these earlier observations. In the previously mentioned cooperative study from Great Britain,[5] 5 of the 18 patients dying in uremia had pathological evidence of an acute or subacute diffuse glomerulonephritis. The incidence of focal embolic nephritis was not given.

In addition, pathological findings on 60 patients dying with subacute bacterial endocarditis[2] at the University of Minnesota Hospital in the twenty-year period from 1939 through 1959 revealed 4 patients with acute glomerulonephritis, 2 with subacute and one with chronic glomerulitis. By contrast, 10 patients were noted to have focal embolic nephritis.

The pancytopenia noted in the present case report is most likely secondary to hypersplenism, although the anemia may be due, in part, to chronic infection. Since splenomegaly,[2,3] for example, a palpable spleen is present in 50% or more of the cases of subacute bacterial endocarditis, disturbances in the hematological picture are not unexpected. In a discussion of mechanisms and treatment of hypersplenism,[11] subacute bacterial endocarditis is mentioned as a treatable cause of splenomegaly with secondary hypersplenism. It is not often appreciated that splenomegaly secondary to infection can produce hypersplenism and pancytopenia. A patient with subacute bacterial endocarditis, splenomegaly, and hypersplenism was recently reported[12] as an example of hypersplenism occurring in infection. While isolated incidences[13] of severe anemia, leukopenia, or thrombocytopenia have occurred, the occurrence of all 3 in one case is unusual.[14,15]

In spite of excellent clinical response to antibiotics, the patient reported died suddenly with intracranial bleeding. A mycotic aneurysm was suspected since they were found at other sites during the autopsy. However, no source for the cerebral hemorrhage could be located. In a series of 16 intracranial mycotic aneurysms[16] subarachnoid bleeding was the initial presenting clinical finding in 14 patients. In 60 autopsies[2] of proved subacute bacterial endocarditis, there were 9 subarachnoid hemorrhages and 5 central nervous system mycotic aneurysms. In a series of 442 patients with subacute bacterial endocarditis reported from England,[5] 17 succumbed from a rupture of a mycotic aneurysm and 16 from cerebral sites.

It is pertinent, however, to note that in a study of the factors affecting the prognosis in bacterial endocarditis,[17] both cerebral embolic and ruptured mycotic aneurysms, if not immediately fatal, carried a surprisingly good prognosis.

SUMMARY

A case of subacute bacterial endocarditis with both azotemia and pancytopenia is reported. The azotemia was due to both a focal embolic nephritis and a diffuse subacute glomerulitis. The latter is properly more common in bacterial endocarditis than is generally appreciated. The pancytopenia was believed to be secondary to hypersplenism. With the increasingly improved prognosis of subacute bacterial endocarditis, it should be included in the differential diagnosis in patients with either renal insufficiency or pancytopenia.

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RETROGRADE INTUBATION of the large intestine can be accomplished with a roll of cellophane tubing that unfolds from within when air is introduced. The tube can be advanced to the splenic flexure and occasionally farther. A long tube of cellophane is tied at one end, and then, starting at this end, the tube is rolled on itself. The tubing is then carefully lubricated with petroleum jelly; the last few inches are everted around the roll and then tied to a short piece of Mayon plastic tubing connected to an air bulb syringe. Pressure on the bulb unrolls the tube forward. Intubation has been used in dogs and studied experimentally in human beings and may prove useful for detecting bleeding or malignant colic lesions, diagnosing large bowel obstruction, and freezing the distal colon.

ODELL COBBIN, ARTHUR J. MADSEN, M.D., EUGENE F. BERNSTEIN, M.D., and OWEN H. WANGENSTEEN, M.D., University of Minnesota, Minneapolis. Preliminary report of a new intestinal intubation principle, with application to the large bowel. Surgery 55:564-566, 1964.

FETAL MORTALITY is reduced in selected cases of transverse presentation by cesarean section and judicious use of external version. Internal podalic version is reserved for the patient in late labor with vaginal delivery imminent or with a dead fetus. Of 101 transverse presentations, cesarean section was done in 48, internal version with breech extraction in 36, and external version in 17. Uncorrected overall fetal mortality rate was 23% and corrected rate 11%. Internal podalic version with breech extraction carried 10 times the risk of cesarean section and 3 times the risk of external version.

CARL E. JOHNSON, M.D., Mayo Clinic and Foundation, Rochester, Minn. J. Amer. med. Ass. 187: 642-646, 1964.

Primary Pulmonary Emphysema in Adolescence

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PULMONARY EMPHYSEMA occurs mostly after the age of 40 and is statistically related to cigarette smoking and exposure to atmospheric pollutants. In patients considered to have pulmonary emphysema, expectoration generally precedes dyspnea by many years.[1] The importance of chronic bronchitis in the pathogenesis of emphysema has been stressed by British workers.[2]

The above-mentioned findings have greatly influenced the formulation of theories concerning the etiology and pathogenesis of emphysema. Any explanatory theory must also, however, take into account unusual forms of emphysema.[3] In a minority of cases, emphysema develops rapidly without any history of chronic bronchitis. Decrease in diffusion capacity compatible with severe damage to the diffusing surface of the lung is a common finding in these cases.[4] Richards[5] has described a form of primary emphysema with bulla formation which he calls "vanishing lung." Seebohm and Bedell[6] reported a series of 10 young men between the ages of 29 and 39 in whom the clinical and physiological findings were compatible with pulmonary emphysema. Most of them complained of cough only after dyspnea had developed. MacLeod[7] described 9 cases with abnormal transradiancy of one lung. Dyspnea was the chief complaint, and cough and sputum were less prominent. Three patients were under the age of 26 years.

We describe a case in a 19-year-old boy compatible with primary, generalized emphysema.

METHODS

Spirometry was done with a low flow-resistance spirometer of Bernstein type[8] with the patient seated. The normal values for vital capacity, forced expiratory volume ($FEV_{1.0}$), and percentage expired (FEV%)[9,10] were obtained in our laboratory. The distribution of ventilation was assessed with the helium wash-in technique of Orinius and Ståhle[11] with the patient recumbent. Simultaneously, functional residual capacity and total lung capacity were determined. Diffusion capacity for carbon monoxide was determined at the physiology department of the Institution of Occupational Health, Helsinki, by using the breathholding technique described by Ogilvie and associates.[12] Arterial oxygen saturation was determined with an Atlas oximeter, and arterial carbon dioxide pressure and pH were determined with a Micro-Astrup apparatus. Blood samples were taken at rest and at the end of six minutes of light exercise (250 kpm/min.) on a bicycle ergometer. Respiratory physiological dead space was computed from expiratory tidal volume, arterial carbon dioxide pressure, and carbon dioxide pressure in expired air, which was analyzed with a Micro-Scholander apparatus. The dead space was measured with the patient seated. Pulmonary arterial pressure was measured with a polyethylene catheter (PE60) and Elema-Schönander pressure transducer.

CASE REPORT

The patient was a 19-year-old boy with no previous history or family history of allergic or respiratory diseases. His health was good during infancy and childhood. At the age of 14 he distinguished himself in a cross-country running race in which several schools competed. He had been smoking 1 to 4 cigarettes a day for three years. There was no history of exposure to dusts. At the age of 14 he developed rhinitis with vasomotor characteristics. At that time he had no cough or shortness of breath. In February 1962, at the age of 17, he joined the army voluntarily. At the beginning of his military service he did not experience any breathing difficulties in spite of participation in strenuous exercise and running. In March 1962, he developed a dry cough, which disturbed his sleep. He was not wheezy and had no dyspnea. In April 1962, he began to cough up much yellow sputum and for the first time experienced shortness of breath during heavy marching. Since that time he has had shortness of breath on exertion. In April 1962, after a hemoptysis, he was taken to a military hospital, where maxillary sinusitis was diagnosed; the pulmonic second sound was accentuated and breath sounds over the right lung were diminished. No asthmatic wheezing was heard. A radiograph of the chest was taken and considered normal. His rhinitis and cough were cured, and he was sent back to the army in July 1962. He still had dyspnea on

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Fig. 1. Chest radiograph (a) and tomogram (b) show increased translucency and attenuation of peripheral vascular markings, especially in the right lung.

exertion. After his military service he worked as a filling-station attendant. In April 1964, he again developed rhinitis and a productive cough with loose yellowish sputum. Shortness of breath became still worse, and in September 1964 he was taken to Laakso Hospital. Before admission he was able to walk only 100 meters on the level without stopping because of dyspnea.

Physical examination. The patient was of slender build. The anteroposterior diameter of the chest was slightly increased. Respiratory excursions and breath sounds were diminished, especially on the right side, and expiration was prolonged. No rhonchi or rales were heard. The pulmonic second sound was accentuated and split. Blood pressure was 115/80 mm. Hg.

Laboratory studies. Most of the leukocytes in the sputum were neutrophils. Pneumococci were cultured from the sputum. The eosinophil count in the peripheral blood was 358 per cubic millimeter. The hematocrit was 50. Serum electrophoresis and immunoelectrophoresis gave normal results. The chloride concentration of sweat was normal (38.5 mEq. per liter). Serum calcium, creatinine, and lipase levels were normal.

X-ray studies. By fluoroscopy, paradoxical movement of the right hemidiaphragm was demonstrated during forced breathing. Inspiratory and expiratory radiographs and tomograms of the lungs showed increased translucency and attenuation of peripheral vascular markings, especially in the right lung (Fig. 1). The hilar shadows were considered normal. Bronchograms showed discrete caliber variation and poor peripheral filling but no gross alteration in the bend geometry of the bronchial tree.

Bronchoscopy. Hyperemia of the bronchial mucosa and abundant mucopurulent secretions in the whole bronchial tree were found. During forced expiration, the posterior wall of the right main-stem bronchus and trachea was invaginated into the lumen, so that the anteroposterior diameter of the right main-stem bronchus was 1 mm.

Respiratory function data (see table). Spirometry showed a pattern of airway obstruction, confined predominantly to the expiratory phase, and increased residual volume with corresponding decrease in vital capacity. The rate of expiratory flow was not enhanced by isoproterenol inhalation or five days of intensive corticosteroid treatment. The helium wash-in was greatly delayed, suggesting grossly uneven distribution of inspired air. As determined by bronchospirometry, the reduction of ventilatory function and pulmonary blood flow as well as air trapping following maximal inspiration was much more pronounced in the right than in the left lung (Fig. 2). The diffusion capacity for carbon monoxide was reduced to less than half of the predicted value. The blood gas values were almost normal at rest. During light exercise, the arterial oxygen saturation decreased to 67%, and the arterial carbon dioxide pressure rose to 57 mm. Hg. The ventilation of the physiological dead space amounted to 52% of the total ventilation. The mean pressure in the pulmonary artery was slightly elevated at rest (22 mm. Hg) and considerably elevated during light exercise (44 mm. Hg).

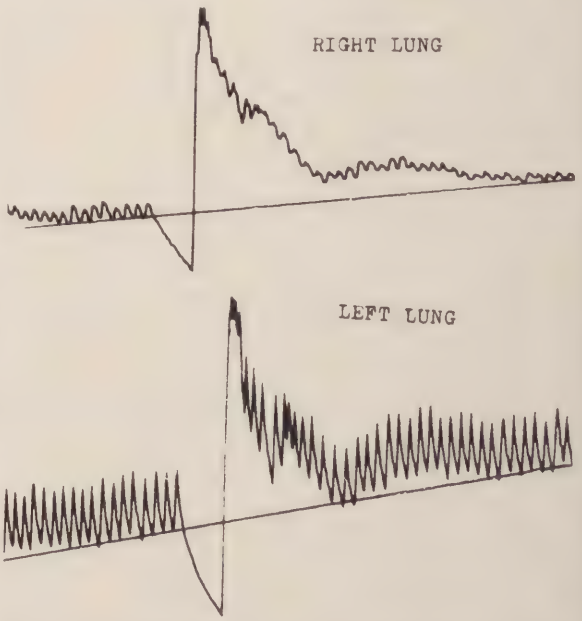


Fig. 2. Bronchospirometry shows that decrease in ventilatory function and oxygen uptake, as well as air trapping, is more pronounced in the right than in the left lung.

RESPIRATORY FUNCTION DATA

	Observed	*Predicted*
Height in cm.	174	
Weight in kg.	53	
VC — ml. BTPS, seated	2,000	5,910
$FEV_{1.0}$ — ml. BTPS, seated	880	4,730
$FEV_{1.0}$ — ml. BTPS, seated after isoproterenol spray	840	
FEV% — ml. BTPS, seated	52	
$FEFR_{200\text{-}1,200}$ — l. BTPS/min.	31	
$MIFR_{200\text{-}1,200}$ — l. BTPS/min.	216	
MVV_{40} — l. BTPS/min.	27	160
RV — ml. BTPS, recumbent	3,910	
FRC — ml. BTPS, recumbent	4,240	
TLC — ml. BTPS, recumbent	6,260	
RV/TLC ratio, % — ml. BTPS, recumbent	62	
HDD (index of helium wash-in) ml. BTPS, recumbent	180	< 20
D_{LCO} (ml./min./mm. Hg) single breath, seated	15.6	36.6
Bronchospirometry, right/left distribution in percent of total function		
VC	45/55	55/45
Ventilation	20/80	55/45
O_2 uptake	35/65	55/45
V_D physiological — ml. BTPS, seated	225	
V_D/V_E ratio, %	52	30
Sa_{O_2}, %, rest	96	
Pa_{CO_2}, mm. Hg, rest	45.5	
pH	7.37	
Sa_{O_2} %, exercise 250 kpm./min., 6 min.	67	
Pa_{CO_2} mm. Hg, exercise 250 kpm./min., 6 min.	57	
Pulmonary artery pressure, mm. Hg, rest		
systolic	34	
diastolic	19	
mean	22	< 20
Pulmonary artery pressure, mm. Hg, exercise, 150 kpm./min., 8 min.		
systolic	58	
diastolic	30	
mean	44	< 30

Clinical examination of the patient's 2 brothers, aged 17 and 21 years, showed no signs of respiratory disease.

DISCUSSION

In the case presented, severe obstructive lung disease developed with remarkable rapidity, apparently in the course of two and a half years. The patient gave no history of intermittent dyspnea or wheezing. Shortness of breath occurred only during physical exercise, and no subjective or objective relief was obtained either from bronchodilating drugs or from corticosteroids. Patient not considered to have bronchial asthma.

Increased translucency of the lungs with decrease in respiratory function may be found when partial atelectasis has caused compensatory emphysema of other parts of the lung. In the present case, bronchography revealed no gross atelectasis. The poor peripheral filling was compatible with infective damage to bronchi and bronchioli.[13] The patient, however, was unable to give any history of bronchopulmonary infective episodes preceding the development of shortness of breath. Symptoms of bronchial infection developed at the same time as the dyspnea. Although there was radiological and bronchospirometric evidence that the changes were most pronounced in the right lung, the poor overall function indicated severe functional disturbance in the left lung, too.[14] The extensive expiratory collapse observed in the right main-stem bronchus and trachea suggested that, in addition to the damage to the lung, there may have been changes in the elastic property of the pars membranacea of the main airways.[15]

In the case presented, a rapid melting away of lung tissue appears to have occurred. The etiology of the process is unknown.

SUMMARY

Rapidly developing primary pulmonary emphysema in a 19-year-old boy is described. Respiratory function studies revealed expiratory airway obstruction, increased residual volume, uneven distribution of inspired air, increased physiological dead space, low diffusion capacity for carbon monoxide, grossly abnormal blood-gas values in the course of light exercise, and pulmonary hypertension. Bronchoscopy showed tracheobronchial collapse.

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The Changing Scene in Medicine 1887-1960

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MY PARTICIPATION in medicine began with my grandfather, Thomas Armstrong, at Sandwich, Illinois, in 1887 or 1888. I was a boy of 14 and Grandfather was a general practitioner in a town of 2,500 people. I regret that I do not know what his education was. If he attended a medical school, it was one of those little schools scattered over the country in his time. I know that he "read medicine" as it was called in those days, with a practicing physician, and was licensed to practice in Illinois when the years of practice act was passed. This act licensed all who were practicing medicine in that state at the time. I believe Grandfather was of the persuasion known as Eclectics, one of the two irregular practices so common then, the other being Homeopathy. These irregular practitioners had succeeded in dubbing the regular school as Allopaths and the name was in general use. Since the Greek "allos" means other, the implication was that these irregular practices were the normal and the regular school of medicine was "other."

Grandfather allowed me to watch him at work with his patients. He had a large practice and visited in the homes. People also consulted him in his own home during certain hours in what I remember as the front parlor. I do not remember that he ever gave a patient a physical examination and know that he had no laboratory. He listened to the account of the patient's symptoms and after this interview would go into a brown study for a short time and then into his little pharmacy, as it might be called. Here were many shelves with beautifully labeled jars of powders, made from various herbs. Taking them one after another, 5, 6, or 7 jars, that he might not miss some of his specifics, he would put a measured amount of each powder into an iron mortar, add some glycerine, and I was allowed to stir this together into an even paste with the pestle. Taking this out, the mass was rolled into a pencil-like column which was placed on a porcelain slab with a measure at one side, numbered up to 30. With a spatula I would cut off each number, making 30 pellets. These would be rolled by a finger into a pill and dropped into a box of licorice powder. Grandfather would take it out to the patient in the waiting room and say, "Take one pill with each meal and come back in ten days."

My father practiced for a time in a nearby community of about 300 people but after three years moved to Sandwich. In the smaller town he had an office on the main street and in Sandwich the office was over the drugstore. Most of his remedies were in pill form and he dispensed them as needed, only occasionally writing a prescription. The drugstore downstairs and the one on the main street were owned and operated by

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a physician, Dr. Winne, although a physician was not at that time licensed as such. He had been an Army surgeon. Many people consulted him and his clerk and were given one or another of the many proprietary remedies of the day. So-called tonics were much in vogue and the most popular was Hostetter's Bitters, probably because it had the largest content of alcohol. In this local option town, Dr. Winne kept a quart bottle of Scotch and a dispensing bottle of bourbon whiskey behind the prescription desk. On the way home from afternoon work the regulars would stop, walk behind the prescription counter with its high, concealing front, pour out a jigger, put down a dime, and take the liquor in one good swallow, seeming hardly to touch the tonsils. One day Ira, the clerk, momentarily left a bottle of similar size containing carbolic acid, mind you, near the other two bottles; a Dr. Dixon, in his haste, picked up the wrong bottle and had the potion down before he could recognize it. He was dead in a few moments. It was his office and horse and buggy which my father bought to begin his practice in that town.

A homeopathic physician, whom we will call Dr. John, was a friendly, voluble man, like the successful politician of this day. When he was called he would tell the patient that it was a pretty serious matter, but he would try his best to bring him out of it. I remember seeing him drive up to his back door, often try to get out of the buggy, but find himself "too many sheets to the wind," climb laboriously back, grasp the reins, turn the horses around, and drive up and down the streets in town at full speed as though they were going to an emergency. When he was sober enough, he would go home. Because of his affability and promises, many people said they would rather have Dr. John drunk than a sober man like my father. The latter did not make so many promises. He dispensed as much cheer and confidence as possible.

Since Grandfather's days I had resolved to study medicine and matriculated at what was then known as the Illinois Industrial University in the school of natural history. The name was soon changed to the University of Illinois. I studied biology, chemistry, physics, physiology, comparative anatomy, and modern languages. In 1891 there were 791 students. I enrolled at the Northwestern University Medical School in the fall of 1894, where it was demanded that a college degree be required for admission. At that time, however, only about 60% of the students complied with this requirement. My premedical sciences were accepted in lieu of my freshman year. During my junior year I lived in a small bedroom in the apartment Dr. Morgan used as his office. He was a practicing surgeon and doubled as professor of surgery, giving lectures and holding clinics in the medical school. Here, I set up a small bacteriological laboratory and wrote a thesis on "Bacteria in Surgery" to fulfill my requirements for the bachelor of science degree at the University of Illinois. I swept out the office and sterilized Dr. Morgan's instruments in an ordinary washboiler. Some of his operations were done in the homes and occasionally by lamplight.

I secured by M.D. degree in June 1897. The work had been mostly by lectures with only an occasional clinic and I observed 4 deliveries handled by Prof. Joseph B. DeLee. After a competitive examination, together with Howard Taylor Ricketts, I entered Cook County Hospital on an eighteen-month service. Here I had such men as Dr. Frank Billings, Dr. James B. Herrick, Dr. Bertrand W. Sippy, and other teachers in the medical schools. My surgical service was with Dr. J. B. Murphy. A few of the attending physicians and surgeons were appointed on a purely political basis. Fortunately, I had very little work with these men. The intern staff consisted of 18 from the regular schools who served for eighteen months each and 6 graduates of a homeopathic school, together with 6 from an eclectic school, each of these serving for twelve months only.

Diagnosis was made on the basis of history, inspection, palpation, and use of the stethoscope. Microscopic examination of blood and urine had reached a very useful stage, but the chemical examination was very sketchy. One illustration might be that in seeking a specific test in typhoid fever we looked for indole and skatole. These names are now forgotten. X-ray diagnosis was unknown. We used the ophthalmoscope and on rare occasions the long hollow needle to secure cerebrospinal fluid. The laryngoscopic mirror was also in use. Cystoscopy, sigmoidoscopy, proctoscopy, and bronchoscopy were yet to come. Generally, fevers were treated as fever and not for the cause, except in malaria. We had many cases of typhoid fever, especially from the camps in the South in 1898. Dr. Herrick sent me to try out the Brand bath treatment. We used a stout sheet as a kind of hammock with a strong man at each end, immersed the patient up to the neck in a tub of water at 50° F., wheeled to the bedside. The body was vigorously rubbed under the water. It was considered dangerous to reduce the body temperature below normal. The

treatment was used daily for a week or so. After 30 cases in which this brutal treatment was used, it seemed evident that no change in mortality or course of the disease was accomplished. Unable to endure the suffering of these patients, I asked Dr. Herrick if I might be permitted to discontinue. Permission was granted.

The surgery of that day was principally that of setting fractures of the extremities, injuries, and of the abdominal and pelvic organs. It was said of one Chicago surgeon that he probably removed more normal ovaries than any man in the world.

During my three months junior surgical and three months senior surgical service, my principal attending surgeon was Dr. J. B. Murphy. He was beginning his brilliant work on the surgery of joints. He was performing entero-enterostomy and gastroenterostomy with the use of the Murphy button. He was also beginning the introduction into this country of artificial pneumothorax. This had been begun by Carlo Forlanini in Italy in 1882, to collapse the lung in cases of cavitation produced by tuberculosis.

Surgery of the heart and lungs was not thought of in those days of inhalation anesthesia. The anesthetics were ether, chloroform, and nitrous oxide.

The superintendent of the hospital, a layman, was a political henchman of Bathhouse John Coughlin and Hinky Dink McKenna, notorious political bosses. We had a remarkable autopsy service under Dr. E. R. LeCount and Dr. W. A. Evans. The former was the physician for the coroner of the county. During my eighteen-month service I was called upon on three separate occasions to act in place of the regular superintendent of the department known as the Detention Hospital. Here, a committee of practicing physicians from the community surveyed, at regular intervals, the number of mental patients sent in for classification. They were classified by the above-mentioned committee according to a long-standing pattern. There was no thought of the origin or of the dynamic study which Freud and others were beginning. The superintendent's absences seven to ten days at a time were due to alcoholic bouts.

I had an illustration of the political influences at work a few days before the end of my service. During the preceding months, word had occasionally been sent from one or the other of the political bosses that an autopsy on a particular person was not to be performed. This had caused a good deal of bitterness on the part of interns and attendants and one or another had gone to the warden's office with recriminations. For some reason, probably because I knew it would be useless, I had avoided this. About three days before leaving to fill my appointment at the University of Minnesota in Minneapolis, I got a summons to the warden's office. I went trembling with fear, knowing that one or two interns had been discharged previously for some infraction and had not secured their certificate of attendance from the hospital. As I entered the warden's office, Mr. Graham said pleasantly, "White, I hear you have a job." I said, "Yes, Mr. Graham, in Minneapolis at the University of Minnesota." He said, "How are you going to get there?" I replied, "I don't know, but I'll get there some way." Pulling a piece of paper out of his pocket, he handed it to me. It was a pass on the Milwaukee Railroad to Minneapolis. "White," he said, "You have done your work and kept your damn mouth shut. This, beside the certificate, is my personal reward for eighteen months of hard work." Interns were not paid in those days. The experience was considered to be full compensation.

Arriving in Minneapolis on the morning of Dec. 1, 1898, I began service as demonstrator of pathology and bacteriology under Dr. Frank Fairchild Wesbrook at the University of Minnesota. I spent the next six years in the laboratory and teaching, advancing gradually to assistant professor. For the next four years I spent part of the time in the laboratory of the university and the late afternoon hours on Nicollet Avenue in the office of Dr. James E. Moore, professor of surgery. Dr. Moore was attending surgeon at several private hospitals and students in small groups, from time to time, attended his clinics there. In 1908 I left Dr. Wesbrook's department and entered that of internal medicine under Dr. Charles Lyman Green, a practicing physician in St. Paul. At this time the movement for a University Hospital had begun and the departments of medicine and surgery were housed separately in two very large residences, one on each side of State Street on Washington Avenue on the site of the newly developed addition to the campus. Here I began a half-time teaching service, spending the other half of the day in private practice downtown.

In 1921, with a full professorship as head of the department of medicine, I also directed the service in medicine at the University Hospital. I continued my half-time salaried position. About 1910 Dr. Wesbrook, who was the dean of the medical school, had a committee of three distinguished medical educators study our medical school, with the particular objective of reporting as to whether heads of the clinical departments

should be whole-time men or part-time. Johns Hopkins Hospital in Baltimore had, some time before, instituted full-time service for the heads of departments. Here were such men as William Osler and William Welsh in medicine and pathology, and the school was rapidly assuming the leadership in medical education and research in this country. Dr. Wesbrook's committee consisted of Dr. Frank Billings of Chicago, Dr. Victor Vaughan, pathologist at the University of Michigan, and Dr. Halstead, head of the department of surgery at Johns Hopkins. In brief, the committee reported that it was not necessary for the heads of clinical departments to be full-time men, although full-time men should be employed in the clinical departments for teaching and research. On assuming my headship, however, in 1921, I had decided to study for myself this question, "Could a man with half-time at the university carry on research as well as conduct a department and teach?" For myself, I resolved that this was not possible, and in 1925 I resigned as the director of hospital service and head of the medical department in order that a full-time man might be employed. This was the beginning of the full-time direction of the departments of medicine at the University of Minnesota. I believe the history of this department and the other departments of the University Medical School fully justify this move. For me, it was a serious break for I had loved my teaching and the contact with patients and students. I had been saddled, however, with so much administrative and committee work that I found it necessary for my own development to concentrate on my practice with the Nicollet Clinic and to retain only a titular connection with the university, giving a few lectures in a field to which I was particularly devoted.

This may be a good place to begin consideration of the progress indicated in the title. Some twenty years before 1887, Louis Pasteur in France had begun his work in bacteriology and immunity. Robert Koch in Germany, in 1882, had cultivated the bacterium of tuberculosis and demonstrated its causative role in the disease. As late as 1894 I had heard Nathan Smith Davis, one of the founders of the medical school which later became Northwestern University, and also a founder of the American Medical Association, declare that bacteria were not the cause of diseases, but its product. Rudolph Virchow was developing the knowledge of cellular pathology. In the 1890s, Marie and Pierre Curie had discovered radium, learned its effect in destruction of tissue, and German scientists had begun its application in medicine. In 1895 Prof. Roentgen also discovered the rays that now bear his name. It took more than fifteen years to produce effective X-ray apparatus, and thus, to begin its application in medicine. In 1880 both my younger brother and I had severe attacks of diphtheria, and at one time I was sent hurriedly to the drugstore to secure some tincture of the chloride of iron which was the remedy then used to shrink the great mass of membrane in the nose and throat. In 1897, while interning in Cook County Hospital, I went to Dr. Ludvig Hektoen's laboratory with a sore throat, from which he secured a smear. Dr. Hektoen stained it, examined it under the microscope, and was able, without a culture, to recognize the bacillus of diphtheria. He gave me an injection of the newly discovered diphtheria antitoxin and I hurried to my home seventy miles away. My father visited me every hour that night and at 4 A.M. I read the delight in his expression as he informed me that the membrane on my throat was beginning to curl at the edges. The next day the membrane peeled off. It was his first experience with an antitoxin.

About three years after my arrival at the University of Minnesota, Dr. Wesbrook, in 1901, had a primitive kind of morgue built for me at the Minneapolis General Hospital, about one and one-half miles from campus. This was in a former box stall for horses in the barn near the large residential building which served then as the hospital. Here, occasional autopsies were performed and recorded numerically, written by hand in a large tome. My teaching and laboratory duties were so heavy that an occasional gap is found in this series because I had no time to write.

About 1904 Simon Flexner, at the University of Pennsylvania, produced a serum curative for epidemic meningitis due to the Diplococcus intracellularis meningitidis of Weichselbaum. Flexner had promptly sent a supply of this serum to the University of Minnesota and it was my good fortune to be the first to administer it here by means of spinal puncture. To see a child mortally ill recover after ten days of this serum and twelve years later have this same boy, a magnificent 6-ft. physical specimen, introduced to me was one of the greatest experiences of my career.

Not long after this, the importance of iodine in the metabolism of the thyroid gland was demonstrated, and later E. C. Kendall in the laboratories of the Mayo Clinic was able to isolate thyroxin. First used therapeutically, and still much in use, was the dried thyroid substance from animals. Later, thyroxin itself was sometimes used in the substitution therapy when a deficiency of the internal secretion of the thyroid

occurred. In the early 1920s substitution therapy had further accessions. Banting and Best in Toronto produced iletin from the islands of Langerhans in the pancreas of animals. A pharmaceutical house purified this and it was marketed as insulin for subcutaneous injections. This dominated the therapy of diabetes mellitus and still has great usefulness. It was only after the discovery of a modification of the sulfa series that another substance effecting a certain control of sugar metabolism has partially replaced it. Shortly after the discovery of iletin, a treatment of so-called pernicious anemia was discovered by Minot and Murphy in the Thorndyke Laboratories at Harvard University. They at first administered chopped liver. Gradually, extracts were produced and, what seems to be the final stage, the isolation of the vitamin B_{12}, which has a limited use in this field. In some cases, because of the almost infinite variety in these maladies, a less purified liver extract is more effective.

About this time, too, intensive study of the lobes of the pituitary demonstrated its role in growth and in the function of water excretion by the kidneys. Thus, substitution therapy began in growth, sexual development, and diabetes insipidus. This little pituitary, weighing less than a gram, has been shown to exercise a great variety of control. One might cite, especially, ovulation, menstruation, and adrenal function. The production of extracts from other animals was one of the great steps in modern therapy. Now and again, a chemist has been able to purify and crystallize an effective substance, and on occasion, to synthesize it. This subject has now become so complex that it would take volumes to enumerate the various triumphs in this field. The story is familiar to the modern physician.

The first electrocardiograph was brought to Minnesota in 1915. The string galvonometer has revolutionized diagnosis in disorders of the heart and brain.

We now approach a field of entirely different character. It is that of antibiotics. For three centuries it had been known that first Cinchonabark, and later quinine, played a part in the cure of malaria. For generations, quinine had been used indiscriminately in all sorts of fevers, it being thought to have a specific effect on them. It was long a favorite remedy for the common cold. It is, I believe, still used and widely advertised in some of the proprietaries dispensed over the counter today. It was about the time of World War II that careful study revealed its effectiveness only on certain stages in the life cycle of certain malarial parasites. Atabrine and some related substances became useful in other stages.

Paul Ehrlich's method of study of chemotherapy was to try out on animals many combinations of slightly varying character. This resulted in the discovery of salvarsan as the six hundred and sixth combination of the arsenicals and it was effective, to a degree, in destroying the spirochete of syphilis. This method has been widely in use since and has resulted in an enormous number of new and effective substances in therapy.

Domagk demonstrated by animal experiments that a product of the analine dyes, sulfanilamide, aided in the control of certain infections. Beginning with this, a great number of products with a sulfa radical have been developed, each with different degrees of effectiveness in various infections. Soon thereafter, Alexander Fleming[1] in the laboratory of St. Mary's Hospital in London, noted that an area occupied by a mold, penicillin, prevented the growth of a staphylococcus. Many others had noted this same phenomenon, but it was Fleming who followed it up. By laborious and extensive culture methods in flasks of broth, he was able to procure a substance known as penicillin. Starting with injections on laboratory animals, he found that this substance had bacteriocidal effect. A London policeman dying with pyemia was treated successfully by injections of this substance. When the supply ran out he rapidly relapsed and died. The story of this "miracle" drug is too long to be telling here, but a brief sketch is worthwhile. Its effectiveness in certain infections in man has been demonstrated.

The British government was asked to undertake its production, but was unable to do so. By a round-about journey, leaving Portugal to avoid destruction by German submarines, two British scientists came to the United States. Here, after some search, it was found that an increase in growth of the mold and production of penicillin could be secured. "Corn steep liquor" was a waste by-product in the making of starch at a factory in Peoria, Ill. Using this liquid, a remarkable increase in growth and productivity of the mold occurred. An extensive search over the world was made and over 1,500 samples of soil were brought by aviators from various lands. Still, all of these molds grew only on the surface of the culture liquid and the production of penicillin was limited and very expensive. One day a girl who had been employed to search the region for any moldy material brought in a moldy cantaloupe and from this the mold grew in depth with again an enormous increase in production of penicillin. In the meantime, one other step of significance had been made. An Italian chemist

learning that the product tended to deteriorate rapidly, devised a method called "freeze drying" which has resulted in a stable product, low in toxicity and at less cost.

Recently, many drugs with tranquilizing and muscle-relaxing action have been found useful. Because of them patients in state hospitals can often be discharged to home or other noninstitutional care, and often to productive lives. The use of these drugs calls for skill and care in observing and recording effects that are toxic as well as beneficial. The story of thalidomide illustrates this point.

This seems to be a good time to comment on the changing role of the physician as related to our culture and his relationship with his patients. In the earlier years before 1900 there were few effective remedies available. The doctor was guided by tradition and his own experience with individual cases. Practice was empirical. Drugs were not tested on animals. As a senior student in 1897 I first heard from Dr. Arthur R. Edwards that the action of belladonna on the sympathetic nervous system had been studied and described in Germany. In 1910 Abraham Flexner for the Carnegie Foundation, with the cooperation of the American Medical Association, announced the results of his survey of the one hundred and sixty-five medical schools of the country. With the elimination of about one hundred unworthy schools, many of which were nothing more than diploma mills, a new era in medical education began. The emphasis was now on scientific developments.

Formerly, the physician visited the homes and dispensed what cheer and courage the circumstances made possible. Hospitalization was seldom resorted to unless surgery was needed. Then, the doctor took or sent his patient to a medical center where specialized services were available. Today every case with any serious implications is admitted to a hospital for diagnostic study since scientific data cannot be obtained under home care. News analyst Eric Severeid brings out the fact that while science must be inhuman and impersonal, its application in the techniques of medicine has long been humanized by the physician. Throughout the history of medicine, from Hipprocates on, the primary consideration of the physician has been the interest and welfare of the patient. The revolution in the medical schools in this country dictated by the Abraham Flexner report of 1910 has, decade by decade, and even year by year, emphasized the role of science and demanded more and more time in its study by the physician. As he has been required to spend more time in his laboratory, in the hospital, and in study, it has seemed to some as if the old-time friend and counselor were a thing of the past. Although he has less time for home visits and the attendant display of personal concern and no longer dispenses his capsules, pills, and tinctures, the true physician, as always, is motivated by the desire for the welfare of his patient and the pursuit of knowledge and excellence which will further this aim. Hospitals with competent medical service have appeared the country over even in small communities and have played their part in the reduction of mortality and the lengthening of the life-span. Today, in most communities, about 96% of the deliveries are performed in hospitals and the reduction this brought about in maternal and infant mortality is one of the great triumphs in medicine.

Accurate dating is almost impossible in this brief sketch but World War II may be used as a starting point in the great increase in activity of rehabilitation and care of the aged.

Thus far, little has been said about surgery. The early surgeon set fractures, drained infected areas where possible, removed cancerous areas usually too late for cure, and knew little of the physiology with which he dealt. Surgery of the appendix and gallbladder are developments of the present century. Anesthesia was by inhalation, principally of ether, chloroform, and nitrous oxide. The use of nerve blocking and regional anesthesia, begun in the first decade of the century, was delayed until nontoxic solutions were developed. Lundy, at the Mayo Clinic, promoted the technique of intravenous methods. Thoracic surgery, impossible during the inhalation era, has progressed since the time of World War II so that the removal of tuberculous or cancerous portions of the lung is an accepted procedure. The closing of an abnormal orifice in the heart and the opening of a stenotic valve or its replacement by a device of foreign material have become commonplace. Aneurysms and closures of arteries can be corrected by taking out the diseased section and inserting an artificial tube of plastic material in which the new vessel lining can grow. When the normal pacemaker fails it has become almost commonplace within the last decade to supply an artificial stimulus from a small battery worn on the surface or buried under the skin.

Through a trephine opening over the parietes, a cannula of approximately 10 cm. in length can be introduced through the cerebral hemisphere, without apparent damage, aimed at a certain nucleus at the base of the brain. A local anesthetic first determines whether the aim has been

correct. Through the cannula, destruction of the nucleus is accomplished. The cessation of the movements and muscle tension of the Parkinson syndrome has been achieved now in thousands of cases. After success on one side of the brain, the opposite side later can be attacked. So far, the speech difficulties common in the syndrome have not been relieved.

How does all this affect the relationship of the physician to his patient and to the community? Instead of treatment in the home, the physician sees his patient in the hospital, the clinic, or his office. Time for intensive study is necessary on his part. It has become almost impossible for the individual physician to keep up with developments even in his own special field, if he has one. Specialization has been a necessity, and nineteen boards for certification in the specialties have been founded. Many men spend at least three years following hospital internship in graduate study of some special field. Thus, great graduate schools have developed where hundreds of graduate students are trained. Research in every field has taken the time and attention of great numbers. Many volumes on this whole subject would be needed to present it factually. A remarkable illustration of this can be seen in Minnesota where the brothers, William and Charles Mayo, in a rural community, Rochester, after acquiring a large following, set up a foundation for study and research which affiliated with the University of Minnesota. Teachers and followers of research have university appointments and titles in the Mayo Foundation at Rochester and the medical school at the University of Minnesota. Each year more than a thousand graduate students may be found in the two institutions occupied in study and research. Training in the specialties may be found in practically every medical school. Research in every field occupies the time of thousands. It has been authoritatively stated that man has acquired more knowledge in a recent decade than had been acquired in all preceding time.

In the early days of this study the physician and surgeon was highly individualistic. There was much misunderstanding with one another and cooperation was not very common. With the rise of specialization the grouping together of men in private practice has developed to a very great extent. Here one works in intimate daily contact with others. Clinical groups may be made with several men in the same special field, or the group may cover all, or nearly all, of the specialties. In either case, better laboratories and other ancillary services can thus be provided. This cooperative effort, in the hospital and in the clinic, putting the experience of one member at the call of all the others, has proved of great value to the patient.

The medical profession with its grass roots organization of county and district societies sending representatives to state associations, and these, in turn, to the national organization, the American Medical Association, has done much to maintain honor and integrity among its members. It has also developed departments serving the whole profession and promoting that pursuit of excellence which we believe characterizes medicine in America today. The medical profession is the most industrious and effective group in the promotion of movements for the public health. It is the hope that we may continue free from the deadening effect imposed by bureaucracy of the centralized state.

It may be said that there is no field of knowledge that has not made some contribution to the medicine and surgery of this day.

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The Journal-Lancet

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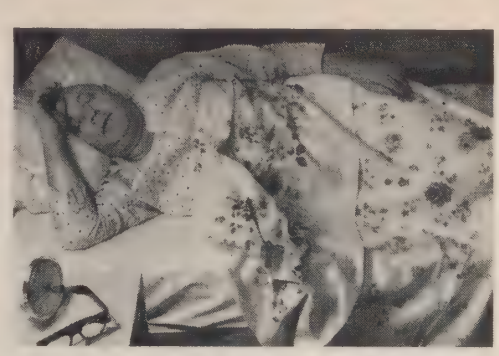
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512214

1. Torosdag, S., Schvartz, N., Fletcher, L., Fertig, H., Schwartz, M. S., Quan, R. F. B., and Bryant, J. M., Pargyline Hydrochloride as an Antihypertensive Agent With and Without A Thiazide, Am. J. Cardiol., 12:822, Dec., 1963.

2. Pollack, P. J., Pargyline Hydrochloride and Methyclothiazide Combined In The Treatment of Hypertension, Cur. Thera. Res., 7:10, Jan., 1965.

3. Bryant, J. M. et al., Antihypertensive Properties of Pargyline Hydrochloride, New Non-Hydrazine Monoamine Oxidase Inhibitor Compared with Sulphonamide Diuretics, J.A.M.A., 178; 406, Oct., 1961.



BP reductions in the recumbent and sitting positions often are nearly as great as in the standing. In clinical trials, the average *recumbent* BP reduction was 36/18 mm. Hg.



The average *standing* reduction in clinical trials was 45/22 mm. Hg. Thus the difference between the standing and recumbent readings was only 9/4 mm. Hg.



Significantly lowers blood pressure in all body positions; less likelihood of orthostatic hypotension

In clinical trials, the average reduction in standing blood pressure was 45/22 mm. Hg.; in the sitting position it was 48/20 mm. Hg.; and in the recumbent position, 36/18 mm. Hg.

Because Eutron effectively reduces blood pressure in all body positions, there is reduced likelihood of orthostatic symptoms or hypotension.

This was reflected in the relatively mild character of side effects seen in clinical trials (see below).

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Onset of antihypertensive action is usually quite smooth. Initial reduction of systolic and diastolic readings is usually seen within a week — maximum reduction in seven to ten days.

Less troublesome side effects may be seen; frequent improvement in "sense of well-being"

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Prescribing information for EUTRON

INDICATIONS: Eutron (pargyline hydrochloride and methyclothiazide) is indicated in the treatment of patients with moderate to severe hypertension, especially those with severe diastolic hypertension. It is not recommended for use in patients with mild or labile hypertension amenable to therapy with sedatives and/or thiazide diuretics alone.

CONTRAINDICATIONS: Eutron is contraindicated in patients with pheochromocytoma, advanced renal disease, paranoid schizophrenia and hyperthyroidism. Until further experience is gained it cannot be recommended for use in patients with malignant hypertension, children (under 12 years of age), or pregnant patients.

The concomitant use of the following is contraindicated: other monoamine oxidase inhibitors; parenteral forms of reserpine or guanethidine; sympathomimetic drugs; foods high in tyramine such as cheese; imipramine and amitriptyline, or similar antidepressants; methyldopa. A drug-free interval of two weeks should separate therapy and use of these agents.

WARNINGS: Pargyline hydrochloride is a monoamine oxidase inhibitor. Patients should be warned against eating cheese, and using alcohol, proprietary drugs or other medication without the knowledge of the physician. When it is necessary to administer alcohol, narcotics (notably meperidine), antihistamines, anesthetics, barbiturates and other hypnotics, sedatives, tranquilizers, or caffeine, these agents can be used cautiously at a dosage of ¼ to ⅕ the usual amount. Avoid parenteral administration where possible. Withdraw pargyline two weeks before elective surgery.

Patients should be warned about the possibility of postural orthostatic hypotension. Those with angina or other evidence of coronary disease should not increase physical activity. Pargyline may lower blood sugar. Potassium depletion is unlikely at the recommended dosage, but if it occurs, adjust dosage or withdraw or provide added natural food sources of potassium; potassium tablets should be avoided wherever possible, as bleeding or obstructive ulceration of the small bowel has been associated with their use; potassium levels should be especially watched if the patient is on digitalis or steroids, or if hepatic coma is impending.

PRECAUTIONS: When determining the antihypertensive effect of Eutron, blood pressure should be measured while the patient is *standing*. Use with caution in hyperactive or hyperexcitable persons. Such persons may show increased restlessness and agitation. Withdraw drug during acute febrile illness. Watch patients with impaired renal function for increasing drug effects or elevation of BUN and other evidence of progressive renal failure; withdraw drug if such alterations persist and progress. Pargyline has not been shown to cause damage to body organs or systems. As with all new drugs, complete blood counts, urinalyses, and liver function tests should be performed periodically. The drug should be used with caution in patients with liver dysfunction. With prolonged therapy, examine patients for change in color perception, visual fields, and fundi.

Elevated blood urea nitrogen, serum uric acid or blood sugar are possibilities attributable to the methyclothiazide in Eutron. Methyclothiazide may also reduce arterial response to pressor amines. Blood dyscrasias, including thrombocytopemia with purpura, agranulocytosis and aplastic anemia, have been seen with thiazide drugs.

SIDE EFFECTS: The use of pargyline may be associated with orthostatic hypotension. Mild constipation, slight edema, dry mouth, sweating, increased appetite, arthralgia, nausea and vomiting, headache, insomnia, difficulty in micturition, nightmares, impotence, delayed ejaculation, rash, and purpura have been encountered with pargyline. Hyperexcitability, increased neuromuscular activity (muscle twitching) and other extra-pyramidal symptoms have been reported. Drug fever is extremely rare. Congestive heart failure has been reported in a few patients with reduced cardiac reserve. Nocturia has been observed with the combination. If side effects persist, despite symptomatic therapy or reduction of the dose, discontinue the drug.

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512214

News Briefs . . .

North Dakota

DR. LESTER D. SHOOK, head of the department of radiology at the Fargo Clinic, has been installed as president of the Rocky Mountain Radiologic Society.

* * * *

DR. JOHN N. ELSWORTH, Jamestown surgeon, has been elected president of the North Dakota Division of the American Cancer Society.

* * * *

DR. RUSSELL O. SAXVIK, Bismarck psychiatrist, has received a distinguished service award from Luther College, Decorah, Iowa, from which he graduated in 1936. Dr. Saxvik is associated with the Quain and Ramstad Clinic, Bismarck.

* * * *

DR. DOUGLAS PYE has opened practice at the Community Clinic, Elgin, in association with Dr. A. A. Curiskis. Dr. Pye, a native of London, England, practiced in Mohall from 1962 to 1964.

MEETINGS, 1966

March, 1966

19 North Dakota Physicians Service Board of Directors (tentative)

30-Apr. 1 North Dakota Public Health Association, Carrington

April, 1966

2 Fargo Clinic Founders' Day, Fargo

29-May 1 79th Annual Meeting – North Dakota State Medical Association, Fargo

30-May 1 Woman's Auxiliary to North Dakota State Medical Association, Fargo

May, 1966

1 North Dakota Physicians Service Corporate Meeting, Fargo

21 North Dakota Heart Association (location undetermined)

June, 1966

12-17 International School of Alcohol Studies—U.N.D., Grand Forks

Minnesota

DR. ROBERT W. GOLTZ, associate clinical professor of dermatology at the University of Minnesota since 1960, has been appointed professor and head of the division of dermatology at the University of Colorado School of Medicine, Denver. Dr. Goltz has been a member of the University of Minnesota faculty since 1951.

* * * *

DR. JURGEN J. MOLLER, Farmington, has taken a residency in anesthesiology at the University of Minnesota Hospitals.

* * * *

DR. HUGH A. STORROW has joined the faculty of the University of Minnesota department of psychiatry and neu-

(Continued on page 20A)



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NEWS BRIEFS

(Continued from page 19A)

rology as a full professor, replacing Dr. Ian W. Gregory, now chairman of the department of psychiatry at Ohio State University, Columbus.

* * * *

DR. HOWARD M. WIKOFF has been elected chief of staff at Bethesda Hospital, Crookston.

* * * *

DR. TARAZOLLAH H. AKHAVAN, pathologist, has been appointed to the staff of the newly established Douglas County Diagnostic Laboratory in Alexandria. The laboratory will provide diagnostic testing and consultation to doctors in Alexandria and adjacent areas. A native of Iran, Dr. Akhavan received his medical degree at the University of Tehran and practiced in Savannah, Ga., before coming to Alexandria.

* * * *

DR. BRANDON L. W. ADAMS, neurological surgeon, has joined Dr. Donald H. Dewey as an associate in the practice of medicine in Owatonna. Dr. Adams graduated in 1963 from the University of Nebraska College of Medicine, Omaha. Since July 1964 he has been assistant resident in neurological surgery at the University of Maryland Hospital, Baltimore.

* * * *

DR. KARL W. ANDERSON, Excelsior, specialist in internal and occupational medicine, has received the Howard S. Diehl award from the University of Minnesota Medical Alumni Association for outstanding service to the medical school, the profession, and the community.

* * * *

DRS. CHARLES M. BAGLEY and DON P. SWENSEN, Duluth, attended a two-day postgraduate course in diagnosis and treatment of cancer held during October at Harvard Medical School, Boston.

* * * *

DR. JOHN G. RAWLAND, anesthesiologist, has joined the staff of St. Ansgar Hospital, Moorhead. A native of Iowa, Dr. Rawland received his medical degree in 1962 from Marquette University and completed his anesthesiology residency there.

* * * *

DR. C. EINER NORBERG, Cloquet physician and surgeon, has received a special award from the Minnesota Synod of the Lutheran Church of America for nine years of service on the synod's board of social ministry.

* * * *

DR. JESSE E. EDWARDS of St. Paul has been elected vice-president of the American Heart Association. Dr. Edwards, an authority on heart pathology, is a former president of the Minnesota Heart Association. He is director of laboratories at Charles T. Miller Hospital, St. Paul, and a professor of pathology at the University of Minnesota Medical School.

* * * *

DR. JOHN W. FODERICK has joined Dr. Herman J. Just in the practice of medicine in Hastings. Dr. Foderick, a general practitioner, received his medical degree from the University of Western Ontario, Canada, in 1941 and practiced in Superior, Wis., before coming to Hastings.

* * * *

DR. ROBERT B. J. SCHOCH, 81, chief health officer of St. Paul for the past thirty-one years, has retired.

(Continued on page 22A)



On Stelazine® brand of trifluoperazine she's calm and alert

When a tranquilizer is needed, 'Stelazine' can regulate the level of anxiety so that the patient is unlikely to overreact to stress but is not tranquilized into psychic inertia. Patients on 'Stelazine' often experience a sense of mental alertness and, because they feel so much better, are more interested in their normal activities.

Contraindicated in comatose or greatly depressed states due to CNS depressants and in cases of existing blood dyscrasias, bone marrow depression and pre-existing liver damage. *Principal side effects,* usually dose-related, may include mild skin reaction, dry mouth, insomnia, fatigue, drowsiness, dizziness and neuromuscular (extrapyramidal) reactions. Muscular weakness, anorexia, rash, lactation and blurred vision may also be observed. Blood dyscrasias and jaundice have been extremely rare. Use with caution in patients with impaired cardiovascular systems.

Before prescribing, see SK&F product Prescribing Information

Photograph professionally posed

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(Continued from page 20A)

DR. DANIEL A. JOHNSON, a general practitioner, has joined the medical staff of the Litchfield Clinic. Dr. Johnson graduated from the University of Minnesota Medical School in 1964.

* * * *

DR. KARL R. LUNDEBERG, retired Minneapolis commissioner of health, has received the Francis E. Harrington award for contributions in public health. The award is given annually by the Minneapolis Junior Chamber of Commerce.

* * * *

DR. ROBERT C. PFEILER, former assistant medical director of the Minnesota Department of Public Welfare, has joined the staff of the American Psychiatric Association in Washington, D. C.

* * * *

DR. ALVIN S. ZELICKSON, dermatologist, has opened practice in Wayzata. He received his medical degree from the University of Minnesota in 1955 and is a member of the American Academy of Dermatology and Syphilology.

* * * *

DR. JAMES M. THOMSON, obstetrician, is leaving Austin after twenty-five years of practice. Dr. Thomson graduated from the University of Minnesota School of Medicine in 1932.

* * * *

DR. HAROLD P. ROBB, psychiatrist and former medical director of the Brainerd State School and Hospital, has joined the staff of the Northern Pines Mental Health Center, Little Falls.

* * * *

DR. REUBEN BERMAN, Minneapolis, has been elected president of the Minnesota Heart Association. Other officers are Drs. Ivan D. Frantz, St. Paul, president-elect, and John L. Juergens, Rochester, secretary.

* * * *

DR. QUENTIN F. KNAUER, general surgeon, has joined the staff of the Sandstone Clinic. Dr. Knauer received his medical degree from Western Reserve University School of Medicine, Cleveland, in 1958.

* * * *

DR. HERB L. HUFFINGTON, Waterville, has been elected president of the Minnesota Academy of General Practice. Other officers are Drs. Edward W. Ciriacy, Ely, president-elect; Chester A. Anderson, Hector, secretary-treasurer; Edward P. Donatelle, Minneapolis, vice-president; Matthew K. Plasha, Coon Rapids, speaker; Wallace E. Mathews, Mankato, vice-speaker; Robert O. Quello, Minneapolis, delegate, and Ellsworth A. Thayer, Fairmont, alternate delegate.

* * * *

DR. RUSSELL O. SATHER of Crookston has been appointed medical director of Sunnyrest Sanatorium, Crookston, to replace Dr. L. H. Flancher, who has retired. Dr. Sather, internist, graduated in 1933 from the University of Minnesota Medical School and is a member of the American Society of Internal Medicine.

* * * *

HEART ASSOCIATION RESEARCH GRANTS totaling $240,000 have been awarded to 20 Minnesota physicians. Included are Drs. Victor Lorber, Minneapolis, Lewis W. Wannamaker, St. Paul, and Earl H. Wood, Rochester, $110,300 to support their work as career investigators of the

(Continued on page 24A)

DEPROL®

meprobamate 400 mg. + benactyzine hydrochloride 1 mg.

Indications: 'Deprol' is useful in the management of depression, both acute (reactive) and chronic. It is particularly useful in the less severe depressions and where the depression is accompanied by anxiety, insomnia, agitation, or rumination. It is also useful for management of depression and associated anxiety accompanying or related to organic illnesses.

Contraindications: Benactyzine hydrochloride is contraindicated in glaucoma. Previous allergic or idiosyncratic reactions to meprobamate contraindicate subsequent use.

Precautions: *Meprobamate*—Careful supervision of dose and amounts prescribed is advised. Consider possibility of dependence, particularly in patients with history of drug or alcohol addiction; withdraw gradually after use for weeks or months at excessive dosage. Abrupt withdrawal may precipitate recurrence of pre-existing symptoms, or withdrawal reactions including, rarely, epileptiform seizures. Should meprobamate cause drowsiness or visual disturbances, the dose should be reduced and operation of motor vehicles or machinery or other activity requiring alertness should be avoided if these symptoms are present. Effects of excessive alcohol may possibly be increased by meprobamate. Grand mal seizures may be precipitated in persons suffering from both grand and petit mal. Prescribe cautiously and in small quantities to patients with suicidal tendencies.

Side effects: Side effects associated with recommended doses of 'Deprol' have been infrequent and usually easily controlled. These have included drowsiness and occasional dizziness, headache, infrequent skin rash, dryness of mouth, gastrointestinal symptoms, paresthesias, rare instances of syncope, and one case each of severe nervousness, loss of power of concentration, and withdrawal reaction (status epilepticus) after sudden discontinuation of excessive dosage.

Benactyzine hydrochloride—Benactyzine hydrochloride, particularly in high dosage, may produce dizziness, thought-blocking, a sense of depersonalization, aggravation of anxiety or disturbance of sleep patterns, and a subjective feeling of muscle relaxation, as well as anticholinergic effects such as blurred vision, dryness of mouth, or failure of visual accommodation. Other reported side effects have included gastric distress, allergic response, ataxia, and euphoria.

Meprobamate—Drowsiness may occur and, rarely, ataxia, usually controlled by decreasing the dose. Allergic or idiosyncratic reactions are rare, generally developing after one to four doses. Mild reactions are characterized by an urticarial or erythematous, maculopapular rash. Acute nonthrombocytopenic purpura with peripheral edema and fever, transient leukopenia, and a single case of fatal bullous dermatitis after administration of meprobamate and prednisolone have been reported. More severe and very rare cases of hypersensitivity may produce fever, chills, fainting spells, angioneurotic edema, bronchial spasms, hypotensive crises (1 fatal case), anuria, anaphylaxis, stomatitis and proctitis. Treatment should be symptomatic in such cases, and the drug should not be reinstituted. Isolated cases of agranulocytosis, thrombocytopenic purpura, and a single fatal instance of aplastic anemia have been reported, but only when other drugs known to elicit these conditions were given concomitantly. Fast EEG activity has been reported, usually after excessive meprobamate dosage. Suicidal attempts may produce lethargy, stupor, ataxia, coma, shock, vasomotor and respiratory collapse.

Dosage: Usual starting dose, one tablet three or four times daily. May be increased gradually to six tablets daily and gradually reduced to maintenance levels upon establishment of relief. Doses above six tablets daily are not recommended even though higher doses have been used by some clinicians to control depression and in chronic psychotic patients.

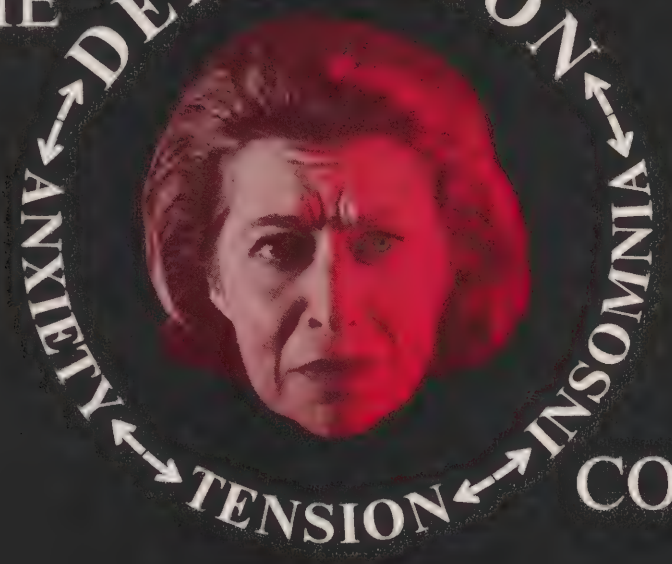
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- Acts rapidly.
- Side effects at recommended dosage infrequent, usually easily controlled.

(Continued from page 22A)

national association; Elia M. Ayoub, streptococcal cell components, $12,100; Ivan D. Frantz, Jr., and Henry Buchwald, effect of ileal bypass on atherosclerosis, $12,-815; Robert A. Good, transplantation, $16,500; Alfred F. Michael, Jr., renal disease, $8,800; Raymond D. A. Peterson, host factors in resistance to infection, $8,800, and Joseph W. St. Geme, Jr., association of mumps virus and heart disease, $12,210. The following physicans have received $2,000 or more: Drs. Jack H. Bloch, Robert S. Eliot, Patrick F. Hagihara, C. E. Harrison, Robert A. Indeglia, Gary W. Lyons, William G. Manax, Bernard Pollara, Harold Richman, and David S. Lirenman.

* * * *

DR. RICHARD B. RAILE, chief of pediatrics at Hennepin County General Hospital, has been appointed medical director, replacing Dr. Thomas Lowry.

* * * *

THE AMERICAN COLLEGE OF CARDIOLOGY will sponsor a symposium on "The Adrenergic Blocking Agents with Special Reference to Hypertension and the Catecholamines" Dec. 4 in the Sheraton-Ritz Hotel, Minneapolis. Visiting faculty will include R. P. Ahlquist, professor of pharmacology and associate dean of the University of Georgia School of Medicine, Augusta, and Karl Engelman, senior investigator with the National Institutes of Health, Bethesda, Md. Local faculty will include Drs. Jesse E. Edwards, St. Paul; Naip Tuna, Minneapolis, and Sheldon Sheps and Richard P. Zimon, Mayo Clinic, Rochester. Cochairmen are Drs. Reuben Berman, Minneapolis, and Dennis J. Kane, St. Paul. Information may be obtained from the executive secretary, American College of Cardiology, 9650 Rockville Pike, Washington, D. C., or from the office of the Minnesota Heart Association, St. Paul.

* * * *

DRS. JOHN T. GOSWITZ and RICHARD J. SNYDER have joined the staff of the Mankato Clinic. Dr. Goswitz, general surgeon, is a 1958 graduate of the Marquette University School of Medicine, Milwaukee, and a member of the American Society of Abdominal Surgeons. Dr. Snyder received his medical degree in 1957 from the University of Cincinnati College of Medicine and is a diplomate of the American Board of Obstetrics and Gynecology and a fellow of the American College of Obstetricians and Gynecologists.

* * * *

DR. GEORGE W. STAHL, Austin, has been elected president of the Southern Minnesota Medical Association. Other officers are Drs. Edmund C. Burke, Rochester, first vice-president; John J. Eustermann, Mankato, second vice-president; and Robert H. Conley, Mankato, secretary-treasurer. The association presented awards to Dr. Donald H. Freeman of the Mankato Clinic for the best case report and to Dr. Jack L. Pulec of Rochester for the best paper.

* * * *

DR. GEORGE M. FARROW, a pathologist, has been appointed an assistant to the staff at the Mayo Clinic, Rochester. Dr. Farrow received his medical degree in 1957 from Louisiana State University School of Medicine, New Orleans. He served with the Air Force Medical Corps and practiced in Elizabethton, Tenn.

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NEWS BRIEFS

DRS. EDWARD L. FOSS and LOUIS A. BRUNSTING have retired from the Mayo Clinic. Dr. Foss, 58, was an instructor in plastic surgery in the Mayo Graduate School of Medicine for fifteen years and was on the staff twenty-two years. He is a member of the American Society of Plastic and Reconstructive Surgery. Dr. Brunsting, 65, was head of the section of dermatology for nine years and was on the staff thirty-five years. He is a member of the American Dermatological Association, the American Academy of Dermatology and Syphilology, and the American College of Allergists.

* * * *

DR. CLARK A. MILLIKAN, head of a Mayo Clinic section of neurology, and 6 other clinic specialists are planning, and will participate in, a nationwide conference on cerebrovascular diseases to be held at Princeton University, N.J., in January. The conference is financed by a joint research grant from the U.S. National Heart Institute and the National Institute of Neurologic Diseases and Blindness. Other members of the planning team are Drs. Jack P. Whisnant, Charles A. Owen, Jr., Robert G. Siekert, Arthur G. Waltz, Robert C. Burton, and Hillier L. Baker, Jr.

* * * *

THE MAYO CLINIC has appointed 6 new staff doctors and 7 assistants to the staff. The new consultants are Drs. John W. Beabout, Jorge E. Maldonado, Edward J. O'Connell, John N. Simons, Lynwood H. Smith, and Ralph S. Zitnik. The 7 new assistants and their specialties are Drs. Richard A. DeRemee, Columba A. Gorman, Miles W. Lynch, and David E. Williams, all internal medicine; Carl E. Dillman, Jr., section of local practice; Theodore L. Sandow, Jr., section of orthopedic surgery, and John C. P. Williams, research in the section of physiology.

* * * *

DR. JOHN T. GOSWITZ has joined the Mankato Clinic staff. For the past two years he was stationed at a U.S. Army hospital in Wurzburg, Germany. Dr. Goswitz, a graduate of the Marquette University School of Medicine, is a member of the American Board of Surgery and the American Society of Abdominal Surgeons.

* * * *

DR. VICTOR C. WELCH, chief of staff at the Veterans Administration Hospital, St. Cloud, has been named director of the Veterans Administration Hospital at Pittsburgh, Pa.

* * * *

DR. IVAN D. FRANTZ, JR., professor of medicine at the University of Minnesota Medical School, has been named president-elect of the Minnesota Heart Association.

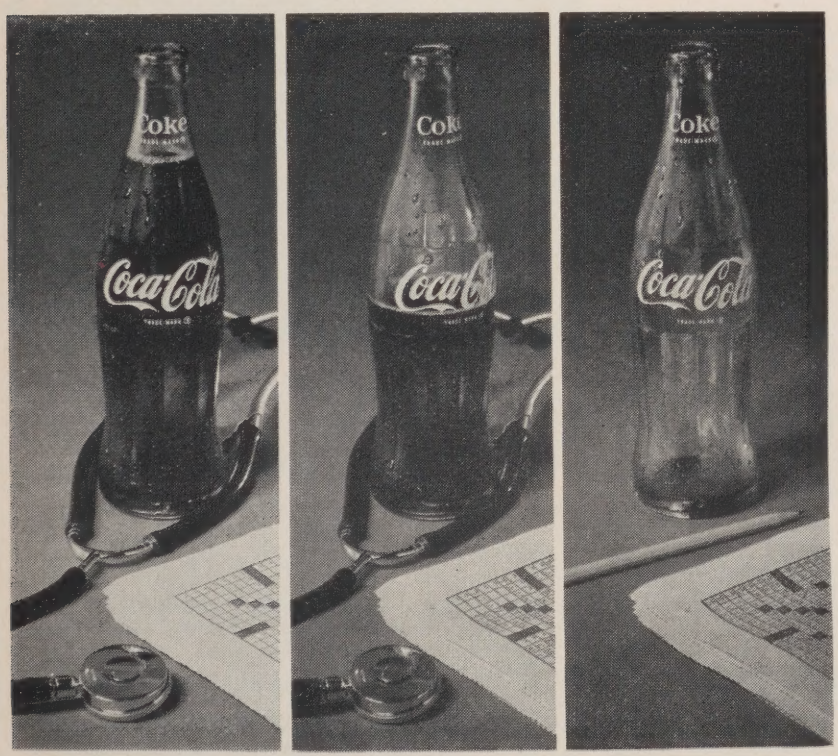
* * * *

DR. ROBERT P. BALDERSON, pathologist at Itasca Memorial Hospital, Grand Rapids, has accepted appointment on a part-time basis at International Falls Memorial Hospital.

South Dakota

DR. MARIO I. HERRERA, a specialist in internal medicine and cardiology, is now practicing in the Professional Arts Building, Aberdeen. Dr. Herrera is a native of San Pedro De Macoris, Dominican Republic, and received his medical degree from the University of Santo Domingo in

(Continued on page 26A)



11:47 pm 11:53 pm 12:06 am

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WANTED—Generalist to associate with two man partnership in Northern Minnesota. Community has a thirty-seven bed hospital with X-ray and laboratory technicians and nurse anesthetist. Good hunting and fishing. Adequate salary and time off. Contact A. G. Janecky, M.D., Baudette Clinic, Baudette, Minnesota.

WANTED—1 or 2 general practitioners. Excellent clinic and hospital facilities. Rural practice established 18 years. Salary open, partnership if compatible. Lloyd H. Klefstad, M.D. Greenbush, Minn.

SACRED HEART, MINNESOTA has been without a doctor since 1961. General practitioner will find suitable building in 700 pop. village, modern hospital 10 miles away; progressive, stable community in west central part of state. Good school, churches. Good family environment. Call or write Rev. Robert Bardy, Telephone 765-2547, Sacred Heart, Minn.

MEDICAL PRACTICE AND EQUIPMENT for sale. Two college town within one hour driving time to Twin Cities. Very good schools. Good hospital. A Mayo trained physician or a man well trained in surgery but willing to do general practice for a few years would fit in best. Reply Box 37 c/o Journal Lancet.

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OPENING FOR PHYSICIAN who is interested in doing surgery and general practice. To work with older surgeon who wishes to retire and one other General Practitioner in small clinic. Reply to C. H. Holmstrom, M.D., Warren Clinic, Warren, Minn. 56762.

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NEWS BRIEFS

(Continued from page 25A)

1957. He has spent two years in residency in internal medicine at the Worcester Memorial Hospital, Worcester, Mass., and two years as a resident in cardiopulmonary physiology at the National Jewish Hospital, Denver. During the past year he has been chief resident in internal medicine at Lakewood Hospital, Lakewood, Ohio.

* * * *

DR. CHARLES F. FALKNER has opened practice in the Emergency room at the Community Memorial Hospital, Murdo, pending completion of the new medical and dental clinic. Dr. Falkner received his medical degree from the University of Manitoba, Canada, in 1952.

Deaths . . .

DR. LUCIUS H. FOWLER, 69, formerly of Minneapolis, died Oct. 13 in Newport Beach, Calif. Dr. Fowler received his medical degree from the University of Minnesota in 1921. He was associated with University of Minnesota Hospital and Northwestern Hospital, Minneapolis, and was an officer of the Hennepin County Medical Society for ten years. He was also a fellow of the American College of Surgeons.

* * * *

DR. JULIUS J. HEIMARK, 77, Fairmont physician for thirty years preceding his retirement five years ago, died Oct. 1 in Phoenix, Ariz. Dr. Heimark graduated from the University of Minnesota Medical School in 1918.

* * * *

DR. LEONARD T. CARLSON, 61, died Oct. 19 in Minneapolis. A 1931 graduate of the University of Minnesota Medical School, he had been medical examiner for the Selective Service Board since 1941 and was a member of the American Academy of General Practice.

* * * *

DR. MAURICE O. PEMBERTON, Deadwood, S.D., died Oct. 4 at the age of 83. Dr. Pemberton received his medical degree in 1912 from St. Louis University School of Medicine, St. Louis, Mo., and came to Deadwood in 1914, where he practiced until his retirement in 1953.

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Contraindications: Ilosone is contraindicated in patients with a known history of sensitivity to this drug and in those with preexisting liver disease or dysfunction.

Side-Effects: Even though Ilosone is the most active oral form of erythromycin, the incidence of side-effects is low. Infrequent cases of drug idiosyncrasy, manifested by a form of intrahepatic cholestatic jaundice, have been reported. There have been no known fatal or definite residual effects. Gastro-intestinal disturbances not associated with hepatic effects are observed in a small proportion of patients as a result of a local stimulating action of Ilosone on the alimentary tract. Although allergic manifestations are uncommon with the use of erythromycin, there have been occasional reports of urticaria, skin eruptions, and, on rare occasions, anaphylaxis.

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WINSTROL combines potent oral anabolic activity with outstanding tolerance, and is remarkably free of side effects. Although its androgenic effect is very low,* women and children should be observed for signs of slight virilization (hirsutism, acne, voice change, and enlargement of phallus or clitoris), and young women may experience milder or shorter menstrual periods. These effects are reversible when dosage is decreased or therapy discontinued, with the exception of voice change and hirsutism which may progress to an irreversible stage on continuation of therapy. Patients with impaired cardiac or renal function should be closely observed because of the possibility of sodium and water retention. Liver function tests may reveal an increase in BSP retention, particularly in elderly patients, in which case therapy should be discontinued. Because anabolic steroids accelerate growth and maturation of bone, precautions should be taken when administered to infants or children in whom full growth and epiphysial closure have not yet occurred. If the bone age and growth of the child are essentially normal the anabolic agent should not be given for more than three months, and then only if there is a clear indication. If growth and bone age are well below normal because of chronic or prolonged disease, continuous therapy may be given for a year or more, provided bone maturation is carefully checked by x-ray studies every three to six months. Since skeletal stimulation may continue for six months after therapy has been stopped, it is recommended that the drug be discontinued well before maturation reaches the norm for chronologic age. *Contraindications:* Although it has been used in patients with cancer of the prostate, its mild androgenic activity is considered by some investigators to be a contraindication. Should not be used during pregnancy. *Dosage* in adults, usually 1 tablet t.i.d.; young women, 1 tablet b.i.d.; children (school age), up to 1 tablet t.i.d.; children (pre-school age), ½ tablet b.i.d. Shows best results when administered with a high protein diet. Available as scored tablets of 2 mg. in bottles of 100.

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